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The MEDICAL DEPARTMENT OF THE UNITED STATES ARMY IN THE WORLD WAR

REFERENCE ONLY

VOLUME XIV

MEDICAL ASPECTS OF GAS WARFARE

PREPARED UNDER THE DIRECTION OF
MAJ. GEN. M. W. IRELAND

The Surgeon General

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LETTER OF TRANSMISSION

I have the honor to submit herewith Volume XIV of the history of the MEDICAL DEPARTMENT OF THE UNITED STATES ARMY IN THE WORLD WAR. The volume submitted is entitled "MEDICAL ASPECTS OF GAS WARFARE."

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PREFACE.^a

In this volume attempt is made to deal with only such problems of gas warfare as concerned the Medical Department directly, or through affiliation with the Chemical Warfare Service. The material seemed naturally to fall into three sections, involving: (1) Organization and administration of the gas service; (2) clinical features of gas poisoning, including certain statistical considerations; (3) experimental researches with respect to the physiology, pathology, and therapeutics of noxious gases.

The connection of the Medical Department with the early development of the defensive aspects of gas warfare has been briefly detailed in Volume I, which gives the administrative history of the Surgeon General's Office. That account is elaborated, with certain necessary repetitions, in the present volume.

Reports by the laboratory investigators concerning the progress of their experimental studies were submitted from time to time during and after the war, many of which formed the basis of contributions which appeared in professional journals or in book form. A considerable part, therefore, of the third, or experimental, section of the present volume has been published. The purpose of this section is to assemble, in one place and in convenient form, the accounts of the work of our most prominent students of the various aspects of gas poisoning, as experimentally investigated.

The immediate editorial supervision of this volume, in the earlier stages of its preparation, and until official orders separated him from the Historical Division, was exercised by Lieut. Col. S. J. Morris, M. C.

^a For the purposes of the History of the Medical Department of the United States Army in the World War, the period of war activities extends from Apr. 6, 1917, to Dec. 31, 1919. In the professional volumes, however, in which are recorded the medical and surgical aspects of the conflict as applied to the actual care of the sick and wounded, this period is extended, in some instances, to the time of the completion of the history of the given service. In this way only can the results of the methods employed be followed to their logical conclusion.

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INTRODUCTION

No attempt is made here to trace the history of gas warfare prior to the entry of the United States into the World War, nor is it intended to dwell upon the work of the other combatants after that time, except as it was concerned directly with our own. The student who may be interested in the evolution of this method of warfare will find it amply covered in published books and in official documents on file in Government bureaus.

The extensive use of poisonous gases was one of the most important military developments of the World War; no innovation since the introduction of gunpowder has revolutionized warfare to such an extent. So seriously did our General Staff regard gas as a weapon that machinery had been put into operation by the end of the war to produce in this country nearly twice as much gas as the combined output of Germany, France, and England.¹ The personnel at Edgewood Arsenal, the chief ordnance plant of the United States Government working on gas, numbered more than 10,000 men and women at the peak of production, and nine other great establishments in this country were engaged in the manufacture of combat gases.² At the time of the armistice these plants were capable of producing 140 tons per day.³

While Germany possessed the advantage of having been the first combatant nation to use poisonous gases, even before Great Britain and her Allies had made a serious study of this subject, the economic conditions in Germany were such that the production of combat gases on a large scale could not be continued throughout the war. Thus, when chemical warfare was first introduced it was estimated that Germany was manufacturing about 50 tons of gas per day, whereas at the time of the armistice she was capable of producing only about one-fourth of this amount.⁴ The rapid development of gas defense and gas production by the Allies promptly deprived Germany of her lead in this phase of warfare. While the Germans originated the manufacture, for war purposes, of most of the gases that were used extensively at the front, all of these gases were soon known to the Allies, whose vast capacity for production quickly turned this powerful weapon of Germany against her own forces.

When Germany launched gas warfare on a large scale against the Allies, the substance selected was the well-known chlorine gas, the first attack being made on April 22, 1915, at Ypres against the French and Canadians.⁵ Enormous numbers of casualties and fatalities resulted at first, but the Allies quickly provided methods of defense. These included strengthening their medical organization to care for casualties produced by this new weapon. The development of a mask, observations regarding the influence of wind, and the exercise of alertness for the singing sound produced by the launching of cylinder or cloud attacks soon enabled the Allies to rob this, the earliest method, of its effectiveness. The same may be said of phosgene, the gas next used by the Germans, and for a time with success. It is true, however, that new gases

of unknown character usually found the opponent unprepared, for the time being, and such gases continued to be effective weapons in each case until specific methods of defense were evolved to meet them. Moreover, with the high development, by the Allies, of protective apparatus against known gases, the enemy constantly sought to obtain better results through the production of new gases and the use of gases of different types during the same attack, hoping that any change would find newly recruited troops of the Allies deficient in gas training and gas discipline.

At the time of our entry into the war the enemy had developed and put into use practically all of the gases employed by them during the war; until the close of hostilities, however, they engaged in further experimentation, and varied both the combinations of gases and the tactics employed in their use.⁶

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SECTION I

ORGANIZATION AND ADMINISTRATION OF GAS DEFENSE

CHAPTER I

ORGANIZATION IN THE UNITED STATES

EARLY HISTORY

The earliest activities of the Medical Department of the United States Army with respect to gas warfare were concerned with furnishing gas masks and other prophylactic apparatus for the Army,¹ rather than with preparations for the care and treatment of gas casualties. The placing of this responsibility upon the Medical Department was the outcome of a meeting of the Board of Ordnance and Fortifications of the War Department, November 5, 1915, when the following was made a matter of record:¹

Certain practices in the present European war have indicated the necessity for providing some equipment of this kind, which, being an entirely new development, does not at present devolve upon any of the supply departments, but, in the opinion of the board, the design and supply should not be left unassigned and should be assigned to the Medical Department.

The Adjutant General of the Army forwarded an extract of the records of this meeting, including the paragraph quoted above, to the Surgeon General, who concurred in the recommendations contained therein.² The Adjutant General then informed the Surgeon General that the Secretary of War approved the recommendations of the Board of Ordnance and Fortification and the Surgeon General as to the development and design of respirators, but reserved decision as to the department which should supply them until further report from the Surgeon General.³

Following the receipt of this communication the Surgeon General assigned certain medical officers to duty with the British and French armies as observers. Reports from these officers which were received from time to time during 1916 included observations on gas defense,⁴ but no actual steps were taken in the matter of furnishing prophylactic apparatus.

The question of responsibility for the supply of gas masks and other gas-defense equipment was brought forward again on February 14, 1917, when the Quartermaster General asked The Adjutant General for information as to which bureau of the War Department would be called upon to furnish gas masks and goggles to the Army should the issue of the same become necessary.⁵

After further correspondence, in which the Chief of Ordnance, The Adjutant General, the Surgeon General, and the Quartermaster General took part,⁶ the matter of responsibility was definitely placed upon the Medical Department on May 4, 1917, when the Surgeon General was informed that the Secretary of War had directed that the Medical Department be charged with furnishing gas masks and other prophylactic apparatus for the Army.⁷

Twelve days later the following memorandum from the Acting Chief of Staff to The Adjutant General was transmitted to the Surgeon General:⁸

The Secretary of War directs that instructions be given for the supply of gas masks, steel helmets, chemical sprayers for cleaning trenches, and oxygen apparatus for resuscitating the wounded as follows:

To the Surgeon General for the supply during the period ending June 30, 1918, of the following articles:

Gas masks	1, 000, 000
Chemical sprayers for cleaning trenches	8, 500
Oxygen apparatus for resuscitating wounded	1, 000

The responsibility was thus clearly placed upon the Medical Department.

At this time no administrative unit in the Surgeon General's Office was charged with matters having to do with execution of this new duty of the Medical Department. Pending the organization of such an activity, a medical officer⁹ represented the Medical Department in all matters concerned with gas defense, on the committee on noxious gases in warfare, formed in the National Research Council in conjunction with the Bureau of Mines of the Department of the Interior.¹⁰

On June 9, 1917, the Surgeon General, in a memorandum to the Secretary of War, outlining the prosecution of the work connected with gas defense, attached the following summary:¹¹

On July 2, 1917, the National Research Council forwarded to the Secretary of War a memorandum stating that at a meeting of the French scientific mission, representatives of the Army and Navy, and members of the General Munitions Board, to discuss the gas question, certain signal points were developed. Among these was the following: "Organization plans for the gas service have already been partially worked out and it remains to draw the units of the organization together. The offensive branch of the gas service is handled by the Ordnance Department, the defensive by the Medical Department, the questions of research by the Bureau of Mines, and the Engineers will probably be charged with the actual handling of the material on the battle field." This memorandum was forwarded by The Adjutant General to the Surgeon General with the information that this action of the meeting, as reported in the memorandum, was approved. In further prosecution of the work in hand it was arranged that the officer in charge of the manufacture and production of gas masks, Ordnance Office, be commissioned in the Sanitary Corps and assigned to active duty at the medical supply depot, New York City, for the purpose of superintending the manufacture, purchase, and inspection of gas masks and other defensive apparatus.

With the apportionment of duties and responsibilities thus definitely settled, the Surgeon General proceeded with the organization, within his office, of the necessary administrative unit for the coordinated management of all matters related to the duties imposed upon the Medical Department, and, on August 31, 1917, by the following office order the Gas Defense Service, subsequently known as the Gas Defense Division, of the Surgeon General's Office, was formally organized:¹²

Under date of May 16 last the Secretary of War directed the Surgeon General to provide for the supply of gas masks, chemical sprayers for cleaning trenches, and oxygen apparatus for resuscitating wounded during the period ending June 30, 1918.

The duty of providing for the supply of these appliances, of repairing them, and of giving instructions in their use is performed by a special field service of the Medical Department, known as the gas defense, the principal office of which is located in this city. It comprises three branches, to wit: (1) Field supply section; (2) overseas repair sections; (3) training section.

The field supply section will purchase or manufacture the appliances named, inspect them, store them, and issue them as needed.

The overseas repair sections will receive issues made in bulk from home country, test them, store them, and issue them to troops, as required; they will also be charged with the disinfecting and repair of used or injured masks abroad, including all necessary inspections and tests incident thereto.

The training section will provide instructions regarding the use of these appliances, the handling of gases used for training purposes, the training of officers and men in the use of gas-sampling apparatus, gas detectors, and other means of defense against gases, and will communicate the same to all concerned.

Col. Weston P. Chamberlain, M. C., until further orders, will be in charge of the Gas Defense Service, with such commissioned and enlisted assistance as may from time to time be assigned thereto.

Until further orders there will be allotted to the Gas Defense Service the following personnel of the Sanitary Corps: 1 major, 28 captains, 115 first lieutenants, 10 hospital sergeants, 64 sergeants first class, 118 sergeants, 71 corporals, 90 privates first class, 334 privates.

PERSONNEL

When the responsibility for the development and production of defensive matériel was placed upon the Medical Department it soon became necessary to supplement the initial personnel allotted to this new activity and to provide trained personnel for the technical and administrative phases of the work, for the supervision of production, for the inspection of the output, for the repair of supplies actually used, for the training of other personnel for these duties, and for the training of the Army as a whole in matters of gas defense, and of Medical Department officers and men for the handling of gas casualties. The trained commissioned personnel was developed chiefly as part of the Sanitary Corps.

From the beginning, however, the Surgeon General experienced difficulty in securing satisfactory personnel for this service.¹³ In an effort to overcome this and to expedite the augmenting of gas defense personnel, the following communication was sent by the Surgeon General to The Adjutant General,¹⁴ in December, 1917:

A large number of men must be commissioned to care for the operation of the new plant authorized in the memorandum of the Secretary of War on November 20. This plant will employ a force of approximately 3,000 people, and all of the inspection work and much of the administrative details must be handled by commissioned officers. It is felt that eventually the whole plant may have to be put on a military basis with no civilian employees as administrative officers.

The Gas Defense Service should have absolute authority to obtain commissions and with such dispatch that men can be assigned within a week after the commission is requested. The Gas Defense Service should also have authority to obtain promotions in the grades of the Sanitary Corps in accordance with the allowances authorized by the Surgeon General.

Acceptance of the plan suggested in the second paragraph of the above communication was denied,¹⁵ and the personnel continued to be obtained in the usual manner.

PRODUCTION

FIELD SUPPLY SECTION

Pursuant to the order creating the Gas Defense Service¹² the field supply section was charged with the purchase or manufacture of gas defense appliances, with inspecting and storing the same, and with issuing them as needed. Included in the list of articles which it thus devolved upon the Medical Department to supply were gas masks for men and animals, trench fans, chemical-testing tubes, vacuum bottles, glass jars for making analyses of gas, weather

vanes, special overalls and suits for protection against certain gases, special gloves for handling articles which might come in contact with dangerous chemicals, and a specially prepared paste for rubbing on the body to protect it against various gases. It also provided supplies for use by the training section in the training camps, such as gas masks, gas bombs, smoke boxes, and various articles for carrying on mimic gas warfare.

The articles enumerated were not procurable in commercial markets, but, at first, were designed by the technical experts of the service or by the Bureau of Mines, working in cooperation with the field supply section,¹⁶ and were made by private manufacturers, under contract from specifications furnished.¹⁷ It was soon found impossible, with this arrangement, to obtain sufficiently rigid inspection to secure a high quality of production, and the establishment of a Government-operated plant was suggested by the officer in charge of the field supply section, Gas Defense Service, New York City.¹⁸ Such a plant was authorized by the Secretary of War, November 20, 1917, at Long Island City, N. Y.¹⁹ At the time of the peak of production this plant had 4,691 civilian employees.

The magnitude of the task imposed upon the field supply section may be gauged by the amount of business transacted in the central office in Washington, as shown in the following report dated March 9, 1918:²⁰

The volume of business done by this organization is growing heavier as progress is made in our manufacturing program. An index to the amount of work done in the office is found in the number of letters coming in and going out daily. One day last week there were 691 letters received and 438 letters sent out from the office, whereas several months ago the daily average was 300 letters received and 200 sent. The largest number of letters received any day so far has been 754 and the largest number sent 684.

The actual output of gas defense material, together with quantities delivered to the Quartermaster Department for shipment overseas, may be found in the Appendix, pages 775, 776.

Of the total number of gas masks, 1,432,224 were delivered to the quartermaster at the port of embarkation for shipment overseas; the remaining 286,408 were used for experiment and training purposes in the United States.

OVERSEAS REPAIR SECTION

As noted heretofore, the order¹² which created the Gas Defense Service provided for the overseas repair section. Accordingly, on October 25, 1917, Overseas Repair Section No. 1 left for France with 4 officers and 110 men of the Medical Department.²¹ The duties, overseas, of this section were to receive issues made in bulk from the United States, to test them, to store them, to issue them to troops as required, to disinfect and repair used or injured masks, and to make the necessary inspections and tests incident thereto.¹²

TRAINING

TRAINING SECTION

On July 24, 1917, The Adjutant General directed the Surgeon General to submit the names of nine officers of the Medical Department for the selection therefrom of three officers for duty as instructors in gas defense in the gas defense school, which was then being organized in connection with the school of musketry of the Infantry school at Fort Sill, Okla.²³ This was promptly

complied with,²⁴ and from time to time Medical Department officers reported for duty as instructors or for training in gas defense at this school. This was the beginning, so far as the Medical Department was concerned, of training in gas defense. It led to the incorporation, by the Surgeon General, of the training section in the plans for the Gas Defense Service,¹² the duties of which were to provide instruction regarding the use of gas defense appliances and the handling of gases used for training purposes; to train officers and men in the use of gas-sampling apparatus, gas detectors, and other means of defense against gases, and to communicate the same to all concerned.

In accordance with the following authorization the field training section proceeded with the organization of division gas schools.²⁵

OCTOBER 3, 1917.

Memorandum for The Adjutant General of the Army:

Subject: Personnel and material for instruction in gas defense.

The Secretary of War directs that the following action be taken:

1. Inform the commanding general of each organized division in the United States to the following effect:

In the establishment of the school of gas defense in your division (see pamphlet on "Infantry Training," August 27, 1917, War Department Document No. 666, page 7, paragraph 4(a)4) the following will govern:

(a) The director of the school will be a qualified medical officer who will be assisted by a chemist and noncommissioned officer of the Medical Corps. Orders will issue from this office directing qualified instructors to report to you for this duty or else you will be informed as to any qualified instructors already on duty with your division.

(b) The Quartermaster General will be directed to construct the necessary gas house for this school. These will be located under your direction.

(c) You will cause the necessary trenches and dugouts to be constructed for the use of this school.

(d) The Surgeon General will be directed to supply the necessary gas masks, chemicals, and other apparatus requisite for the course.

(e) You will continue the courses in this school until every officer and enlisted man in your division has taken the course.

2. Inform the Quartermaster General that the Secretary of War authorizes the creation of a deficit in the sum of not to exceed \$40,000 for the construction of suitable gas houses, for instruction in gas defense, and direct him to undertake this construction, according to plans on file in the office of the Surgeon General, at each divisional training camp in the United States, under the direction of division commanders. The completion of this construction at the earliest practicable date is to be desired.

3. Inform the Surgeon General that a school of gas defense is to be established in each divisional camp or cantonment in the United States and that the Quartermaster General will be directed to construct the necessary gas houses for each of these schools, and that all officers and enlisted men in each division are eventually to take the course in these schools.

Direct him to furnish each of these schools with the necessary gas masks, chemicals, and other apparatus requisite for the course of instruction in gas defense, and to furnish the Quartermaster General with the necessary plans for the construction of gas houses.

4. After consultation with the Surgeon General, you will issue such orders as are necessary to place on duty with each organized division in the United States at least one medical officer, one chemist, and one noncommissioned officer of the Medical Corps, all of whom shall be designated by the Surgeon General as being qualified to act as instructors in the schools of gas defense.

5. You will inform the commanding general of each organized division in the United States of the names of the officers, chemists, and noncommissioned officers of the Medical Corps who are qualified to act as instructors in gas defense and who are now on duty with their respective divisions or who have been ordered to join.

In October and November, 1917, details of British officers experienced in gas defense warfare arrived in Washington. These officers were sent to the

various cautions to assist in the organization of gas defense schools.^a (See Appendix, p. 777).

Schools for instruction in gas defense were organized in the various divisions in accordance with orders.²⁶ The director of the school in each division was a medical officer, assisted by a chemist and a noncommissioned officer of the Medical Corps. An illustration of what was done in the way of instruction in the division may be found in the Appendix (p. 778.)

TRANSFER TO ENGINEERS

On February 27, 1918, the commissioned personnel of the field training section, with the exception of four officers, was transferred to the Engineers, National Army.²⁷ In April the remainder of the personnel was placed in charge of the Chief of Engineers, pursuant to a memorandum from the Chief of Staff, which assigned the reasons for the transfer:²⁸

1. When instruction in gas defense was first undertaken and a gas school established at Fort Sill, Okla., it was the intention to detail line officers to take the course there with a view to their subsequent assignment to divisions as divisional gas officers, and in charge of the divisional gas schools.

It was, however, not practicable to secure the necessary line officers, so recourse was had to medical officers then available. These medical officers were given a course of instruction at this gas school and then assigned to the various National Army and National Guard divisions.

A number of chemists were given a course of training at the American University in Washington, D. C., and assigned to divisions as chemical advisors to the medical officers in charge of the gas schools. This was in accordance with the provisions of W. P. D. 9967-11, dated October 3, 1917. There were 33 medical officers and 32 chemical advisors so assigned. In addition 12 chemical advisors were, by request of General Pershing, sent to France.

2. Soon after the arrival here of the British officers, advisers in training in gas warfare, the question came up as to whether or not it would be more advisable that gas officers should belong to the line rather than to the Medical Corps, as their duties abroad would be distinctly combatant and inasmuch as medical officers were classed as noncombatants.

From the training standpoint it appeared much more desirable to have a line officer rather than a medical officer in direct charge of the division gas school and gas instruction.

These chemical advisers were accordingly recommissioned in the Engineer Officers' Reserve Corps (W. P. D. 9967-34, Jan. 21, 1918), with the intention of designating them as chief gas officers of divisions, thus relieving medical officers.

The transfer having been made complete, the field training section of the Gas Defense Service ceased to be a Medical Department activity.

More complete details of training for gas defense will be found in Volume VII, on education and training.

SANITARY SUPERVISION OF GAS FACTORIES^b

When the manufacture of war gases in this country was decided upon, the necessity of protecting the operatives in factories and filling stations became apparent. Foreseeing the dangers of large-scale, high-speed production of the war gases, the director of the experimental physiological laboratory of the Bureau of Mines, who was in charge of the physiological problems connected

^a Maj. S. J. M. Auld, chemical adviser, British military mission, who was of great service in developing methods of training and furnishing information and suggestions, prepared, for use by the training section and in the gas defense schools, the following pamphlets: Gas Warfare: Part I. German Methods of Offensive. Part II. Methods of Defense Against Gas Attacks. Part III. Methods of Training in Defensive Measures.

^b The discussion of this subject is based on a final report by Capt. H. C. Bradley, S. C. (later major, C. W. S.), who organized the section at the suggestion and under the direction of Dr. Yaddell Henderson, Director of the experimental physiological laboratory of the Bureau of Mines, and who was in charge throughout its existence.

with war gases, suggested adding this activity to the Medical Division of the Bureau of Mines. This recommendation was approved by the Director of the Bureau of Mines of the Department of the Interior and an officer was detailed to the work.²⁹

At first it was thought that the cost of protection of operatives in gas manufacturing and filling plants was an essential part of the cost of production and could be so charged off; but in attempting to secure the services of a local physician as a regular inspector of a plant, it was discovered that the Ordnance Department could not arrange for his remuneration or for the payment of hospital fees. At the same time contracts had been made with the manufacturing agents relieving them of all responsibility for protection, and making the Government liable.³⁰ The whole question, therefore, was placed before the Surgeon General of the Army, with a request that protection in these factories be undertaken by the Medical Department. In view of the fact that part of the personnel operating these plants and inspecting the products were soldiers, the Surgeon General undertook to furnish the required protection.

The plan for this service provided for the appointment of local physicians as contract surgeons, whose duty it was to hold sick call, give physical examinations at regular intervals, examine applicants for work in the gas plant, and to be available for emergency calls at all hours. Both Army and civilian personnel were treated by these contract surgeons. Arrangements were made with local hospitals to handle cases, and emergency rooms, wards, and offices were provided at the ordnance plants, and equipped by the Supply Division of the Surgeon General's Office.

When the field problem of gas-plant protection was undertaken by the Surgeon General, the existing organization in the Bureau of Mines having to do with this work was taken over in full. The factory protection section of the Gas Defense Service thus came into being as an activity of the Surgeon General's Office, and from February to June, 1918, the organization was about as shown in Chart I.

The work undertaken by the section fell into the following categories:

1. Research service: (a) On the chronic effects of low-concentration war gases; (b) protective devices; detectors, especial garments, etc.; (c) therapy.

2. Field service: (a) Selection, appointment, and training of contract surgeons and medical officers; (b) installation of emergency ward, dispensary and first-aid equipment; (c) inspection.

3. Educational service: (a) Collection of reports, case histories, and information; (b) preparation of bulletins of information for medical officers and contract surgeons; (c) assignment of problems for solution in laboratories; (d) development of special course of instruction at American University for medical officers, to be used later in factory instruction and assigned to the large plants for duty.

This plan involved the building up of a central office in charge of factory protection, whose function it would be to collect and disseminate information, serve in liaison capacity between laboratory and factory, and compile and interpret the case histories from the various medical officers connected with the gas plants.

The functions of this office rapidly expanded during the spring of 1918 and it became the clearing house for information of a medical character developed in the various collaborating organizations. A medical advisory board,

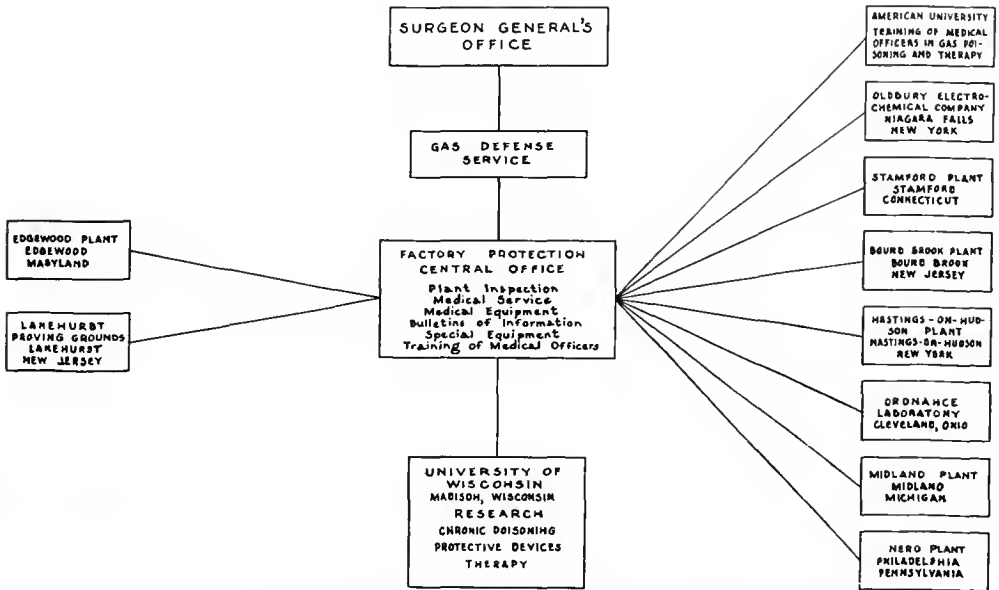


CHART I.—Factory protection section, gas defense service, Surgeon General's Office

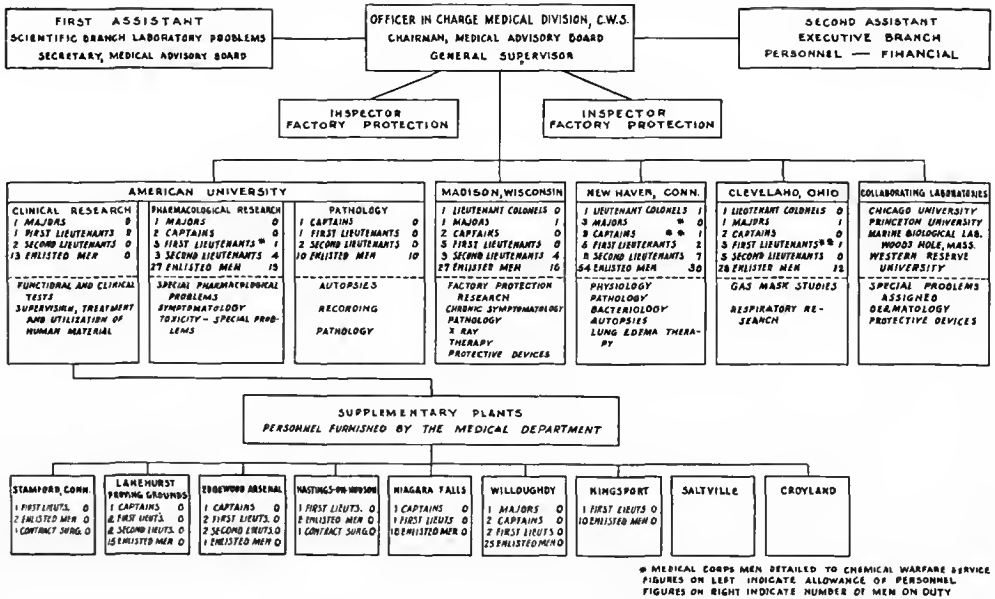


CHART II.—Medical Division, Chemical Warfare Service, July, 1918

consisting of representatives of these laboratories, met in Washington each month to report progress of research and to assign new problems. The organization at the time of transfer to the Chemical Warfare Service and from then to the close of the war was about as indicated in Chart II.

TRANSFER TO CHEMICAL WARFARE SERVICE

With the transfer of the Gas Defense Service as a whole to the Chemical Warfare Service the work of factory inspection ceased to be a Medical Department activity, although carried on by Medical Corps officers detailed to service with the Chemical Warfare Service.

RESEARCH^c

ORGANIZATION IN THE BUREAU OF MINES

In February, 1917, the Director of the Bureau of Mines called the attention of the War Department to the already existing technical organization in the bureau for the study of poisonous gases in mines and offered these facilities to the War Department for work on noxious gases in warfare. A meeting was arranged between representatives of the Bureau of Mines and the War College. The War Department accepted the offer of the Bureau of Mines and agreed to support the work in every way possible.

The research work thus inaugurated was carried on with the funds of the Bureau of Mines until July 1, 1917, after which funds were supplied by the War Department and the Navy Department.

On April 6, 1917, the committee on noxious gases in warfare of the Council of National Defense, in cooperation with the Bureau of Mines, was organized, under the chairmanship of the Director of the Bureau of Mines, and with an officer from each of the following: Ordnance Department, United States Army; Medical Department, United States Army; Bureau of Ordnance, United States Navy; Bureau of Medicine and Surgery, United States Navy; department of organic chemistry, Columbia University, New York City; Bureau of Chemistry, United States Department of Agriculture. The committee was subsequently reorganized with representatives of the following: Bureau of Mines (director as chairman of committee); science and research division, National Research Council (three members, ex officio); Bureau of Chemistry, United States Department of Agriculture; Corps of Engineers, United States Army; Gas Defense Service, Surgeon General's Office; Bureau of Medicine and Surgery, United States Navy (two members); Ordnance Department, United States Army; Bureau of Ordnance, United States Navy.

After the literature on gas warfare received from France and England had been digested, definite lines of research were mapped out.

It was felt by the committee that the most important work had to do with the development of gas masks for the Army. This meant studying charcoal, soda lime, and the various mechanical parts of the mask, such as the facepiece, elastics, eyepieces, mouthpieces, nose clips, hose, cans, valves, etc.

Work was started at the Bureau of Mines, Pittsburgh, Pa. It was soon deemed advisable to separate the manufacturing from the research end, and this was accomplished with the organization of the Gas Defense Service in the Office of the Surgeon General.

The research staff grew so rapidly that sufficient laboratories were not available in Washington or in any other one place. Before long, research work was being carried out at the Bureau of Mines, Pittsburgh, Pa.; the National Carbon Co., Cleveland, Ohio; the Forest Products Laboratory, Madison, Wis.:

^c The discussion of this subject is based on the History of the Chemical Warfare Service in the United States, by Lieut. Col. W. D. Bancroft, C. W. S., Part I, May 31, 1919. Copy on file, Historical Division, Army War College.

the University of Chicago; the research laboratory of the American Sheet & Tin Plate Co., Pittsburgh, Pa.; the Bureau of Chemistry laboratory, Washington, D. C.; the Yale Medical School laboratory, New Haven, Conn.; the Massachusetts Institute of Technology, Cambridge, Mass.; the Mellon Institute, Pittsburgh, Pa., and elsewhere. In the summer of 1917 the American Methodist University offered its buildings and grounds, rent free, for research purposes. After the necessary reconstruction, these laboratories became available in September, 1917, and the institution then became known as the American University Experiment Station of the Bureau of Mines. The organization at that time included divisions from the following activities: Gas investigations; defense problems; medical science problems; chemical research; gas mask research; pyrotechnic research; small-scale manufacturing; mechanical research; pharmacological research; administration. Branch laboratories were organized from time to time at the Catholic University of America, Washington, D. C.; Johns Hopkins University, Baltimore, Md.; Princeton University, Princeton, N. J.; National Carbon Co., Cleveland, Ohio; Nela Park, Cleveland, Ohio; Harvard University, Cambridge, Mass.; Yale University, New Haven, Conn.; Wesleyan University, Middletown, Conn.; Ohio State University, Columbus, Ohio; Bryn Mawr, Pa.; Massachusetts Institute of Technology, Cambridge, Mass.; Cornell University, Ithaca and New York City, N. Y.; University of Michigan, Ann Arbor, Mich.; Clark University, Worcester, Mass.; Worcester Polytechnic Institute, Worcester, Mass.; University of Wisconsin, Madison, Wis.; Sprague Institute, Chicago, Ill.; and Ordnance Proving Ground, Lakehurst, N. J.

TRANSFER TO CHEMICAL WARFARE SERVICE

Work was prosecuted in the various laboratories along the lines undertaken by each, under the immediate supervision of the Bureau of Mines and its central laboratory at American University, until July, 1918, when the Chemical Warfare Service was organized. All research activities, personnel, and equipment were then transferred to the new service, along with the Gas Defense Service of the Medical Department.

Medical Department commissioned personnel was detailed to the work as requested, and at all times the Surgeon General was in touch with the experiments being conducted. With the organization of the Chemical Warfare Service, as noted, the Medical Department personnel, consisting chiefly of Sanitary Corps officers, was detailed to the new service or recommissioned in the Chemical Warfare Service. The Medical Division of the new service was placed under direction of an officer of the Medical Corps.

The maximum research staff was about 1,900, consisting of 1,200 technical men and 700 service assistants. The latter included stenographers, clerks, accountants, purchasing agents, machinists, instrument makers, and others.

Certain phases of the research work conducted along the lines indicated, which was of particular interest to the Medical Department, are discussed in Section III.

TRANSFER TO CHEMICAL WARFARE SERVICE

With the organization of the Chemical Warfare Service²² all personnel, property, obligations, and funds were transferred to the new service, and gas defense ceased to be a function of the Medical Department.

REFERENCES

- (1) Memorandum from The Adjutant General to the Surgeon General, November 18, 1915. On file, Record Room, S. G. O., 153462 (old files).
- (2) Second indorsement, the Surgeon General to The Adjutant General, November 22, 1915. On file, Record Room, S. G. O., 153462 (old files).
- (3) Fifth indorsement, The Adjutant General to the Surgeon General, December 7, 1915. On file, Record Room, S. G. O., 153462 (old files).
- (4) Reports from observers on gas defense. On file, Record Room, S. G. O., 150021 (old files).
- (5) Letter from the Quartermaster General to The Adjutant General, February 14, 1917. On file, Record Room, S. G. O., 156296 (old files).
- (6) Second indorsement, February 19, 1917, the Surgeon General to the Chief of Ordnance; third indorsement, Ordnance Office to The Adjutant General, April 7, 1917; first indorsement, the Quartermaster General to the Surgeon General, April 9, 1917; second indorsement, the Surgeon General to the Quartermaster General, April 12, 1917; third indorsement, the Quartermaster General to The Adjutant General, April 14, 1917. On file, Record Room, S. G. O., 156296 (old files).
- (7) Third indorsement, The Adjutant General to the Quartermaster General, the Chief of Ordnance, and the Surgeon General, May 4, 1917. On file, Record Room, S. G. O., 156296 (old files).
- (8) Memorandum from the Acting Chief of Staff to The Adjutant General, May 16, 1917; first indorsement, The Adjutant General to the Surgeon General, May 16, 1917. On file, Mail and Record Division, A. G. O., 2598068 (old files).
- (9) Orders (S. G. O.), April 7, 1917. Subject: Maj. Llewellyn P. Williamson, M. C. On file, Record Room, S. G. O., 50163 (old files).
- (10) Summary of the work of the Bureau of Mines on Noxious Gases, June 9, 1917. On file, Record Room, S. G. O., 156296 (old files).
- (11) Memorandum from the Surgeon General to the Secretary of War, June 9, 1917. On file, Record Room, S. G. O., 156296 (old files).
- (12) Orders (S. G. O.), August 31, 1917. On file, Record Room, S. G. O., 201948 (old files).
- (13) Correspondence, Subject: Personnel for Gas Defense Service. On file, Record Room, S. G. O., 201948 (old files). Also: Weekly Reports, Field Supply Section, Gas Defense Service, Surgeon General's Office. On file, Weekly Report File, S. G. O.
- (14) Letter from the Surgeon General to The Adjutant General, December 20, 1917, pars. 4 and 6. On file, A. G. O., 426.4.
- (15) Third indorsement, The Adjutant General to the Surgeon General, January 11, 1918. On file, Mail and Record Division, A. G. O., 426.4.
- (16) Weekly Reports, Field Supply Section, Gas Defense Service, Surgeon General's Office. On file, Weekly Report File, S. G. O.
- (17) Weekly Reports, Field Service Section, Gas Defense Service. On file, Weekly Report File, S. G. O.
- (18) Letter from officer in charge, Field Service Supply Section, Gas Defense, to the Surgeon General, November 17, 1917. On file, Mail and Record Division, A. G. O., 426.4 (E. E.).
- (19) Memorandum, War Department, to the Secretary of War, November 20, 1917; approval by the Secretary of War, November 20, 1917. On file, A. G. O. 426.4 (E. E.).
- (20) Weekly Report, Field Supply Section, Gas Defense Service, March 9, 1918. On file, Weekly Report File, S. G. O.
- (21) Letter, from officer in charge, Gas Defense Service, to Surgeon General, October 5, 1917. Subject: Overseas Repair Section. On file, Record Room, S. G. O., 210189 (old files). Confidential Order No. 92, War Department, pars. 7 and 14, October 11, 1917. On file, Confidential Orders, Commissioned Personnel Division, S. G. O.
- (22) G. O. No. 62, W. D., June 28, 1918.
- (23) Letter from The Adjutant General to the Surgeon General, July 24, 1917. Subject: Instructors at the School of Musketry. On file, Record Room, S. G. O., 193166 (old files).
- (24) First indorsement, from the Surgeon General, United States Army, to The Adjutant General, August 2, 1917. On file, Record Room, S. G. O., 193166 (old files).

- (25) Memorandum for The Adjutant General of the Army from the Chief of Staff, October 3, 1917. Subject: Personnel and material for instruction in gas defense. Copy on file, Historical Division, S. G. O.
- (26) Memorandum for the Chief of Staff from Col. J. J. Bradley, General Staff, Acting Director of Training, January 21, 1918. On file, Chemical Warfare Service, File No. 353.5.
- (27) S. O. No. 48, W. D., pars. 258 and 259, February 27, 1918.
- (28) Memorandum for the Chief of Staff from Col. D. W. Ketcham, War Plans Division, Acting Assistant Chief of Service, General Staff, from Acting Director, W. P. D., A. A. C. of S., April 6, 1918. Subject: Gas Training. On file, Chemical Warfare Service, 353.9. A. G. S. O. 3, C. W. S. $\frac{3.5}{2} \frac{3}{8} .5$.
- (29) Order, Bureau of Mines, November 27, 1917, creating the Medical Division, and placing Dr. H. C. Bradley in charge of sanitary supervision of gas factories. Copy incorporated in final report (Factory Protection in the War Gas Plants) of Major Bradley. On file, Historical Division, S. G. O.
- (30) Indemnity clause in contract for construction and operation of gas plant on cost-plus basis. Copy included in Major Bradley's report on Factory Protection in the War Gas Plants. On file, Historical Division, S. G. O.

CHAPTER II

ORGANIZATION IN THE AMERICAN EXPEDITIONARY FORCES

EARLY HISTORY

Early in 1917, prior to declaration by this country of war with Germany, arrangements were made with the French Government for two medical officers, who had been on duty as military observers with the allied forces since 1915 and 1916, respectively,¹ to attend the French Army school of asphyxiating gases, then in session at Paris. After taking the full course of instruction at the school, one of these officers submitted a full and comprehensive report to the War College, in Washington.² This was the first complete report relative to gas warfare received by the War Department.²

On the completion of this work one of these officers decided to go as far as possible in informing himself on the subject of gas warfare.² Through the influence of officers in the French gas school he was appointed an unofficial liaison officer with the French gas service. In this capacity he had ready access to the offices of this service, to the experimental proving grounds at Fontainebleau and near Versailles, and to the various factories, and was furnished with many statistical reports of great value.

Following the arrival in France of General Pershing, in June, 1917, and the merging of our military mission to France into his staff,³ this medical observer was directed to report to the commanding general, American Expeditionary Forces, for instructions.⁴ He was then (June, 1917) assigned to duty with the chief surgeon;⁵ a little later he was ordered to assist the officer temporarily in charge of the Gas Service,⁶ and, on the return of this officer to the United States, was verbally delegated to act as chief of the Gas Service, pending the arrival of the Engineer officer to be designated to organize the Gas Service.^{2,7}

In the meantime another of our medical officers had been detailed to study the physiological aspects of gas warfare with the British.⁸ He carried with him to Headquarters, American Expeditionary Forces, a large number of valuable and instructive reports and documents, which, together with those already in the hands of the acting chief of the Gas Service, furnished a skeleton of practically the entire system of gas attack and defense as employed by the British and the French. Other medical officers detailed for special duties with respect to studying gas warfare submitted additional reports.⁹

The preliminary study thus made by our medical officers of the work of our allies laid the foundation for the comprehensive suggestion for an organization, together with a chart of the same, prepared for the chief of staff, American Expeditionary Forces, July 26, 1917, by an officer of the Medical Corps. (See Appendix, p. 797).^a

This plan was finally approved, on August 13, 1917, as a basis of organization, and its author was authorized to put such features of the plan into effect

^a The "Gas defensive organization of the British armies in France" and an "Abstract of plan for organization of gas service in U. S. Army," submitted by Maj. Charles Flandin, of the French gas services, dated July 30, 1917, are given in the Appendix (pp. 804 and p. 806, respectively).

as were necessary under existing conditions.¹⁰ Final approval of the whole plan was held in abeyance until the chief of the Chemical Warfare Service was designated and assigned to the duty.¹⁰

ORGANIZATION OF GAS SERVICE

When, on July 5, 1917, the Gas and Flame Service, as the Gas Service was then called, was designated as one of the staff corps of the American Expeditionary Forces, its duties included the following:³ Supply and control of personnel; procurement of supplies and material; conduct of entire Gas and Flame Service, both offensive and defensive; supervision of instruction of gas troops and officers; inventions and experiments of gas apparatus; experiments on gases of all kinds; experiments on gas protection; control of gas laboratories.

The relationship of the Gas Service to other departments is shown in the following:³ From the Corps of Engineers it obtained the supply of personnel and material for gas and liquid fire offensive, except those furnished by other services; from the Medical Corps, the supply of personnel and material for gas defensive under supervision of Director of Gas Service; from the Ordnance Department, the supply of gas bombs, gas shells, and other similar material for gas service.

On August, 17, 1917, an officer of the Corps of Engineers was appointed as "Engineer in charge of gas." ¹¹ The medical officer attached to the chief surgeon's office who had been acting chief of this service was assigned to the chief of the service as medical director on August 22, 1917.¹² At that time little progress had been made toward effecting a definite organization. (See Appendix p. 810.) On September 3, 1917, a definite step in that direction was taken:¹³

* * * * *

IV. 1. There is established a department of the American Expeditionary Forces to be known as the Gas Service.

2. The head of this department will be designated as chief of the Gas Service and will be charged with the organization of the personnel, the supply of material, and the conduct of the entire Gas Service, both offensive and defensive, including instruction.

3. The organization of the service will be as indicated in the table attached hereto.

4. All material and appliances that may be needed by the Gas Service will be supplied by those departments of the Army usually furnishing such supplies and appliances.

5. The supply of material for the Gas Service will be made directly to the supply and depot services of that organization by the departments concerned.

By command of Major General Pershing:

(Signed)

JAMES G. HARBORE,
Lieut. Col., General Staff,
Chief of Staff.

Official:

BENJ. ALVORD,
Adjutant General.

RELATIONSHIPS OF THE MEDICAL DEPARTMENT TO GAS WARFARE

While, as is shown in Chart III, a special service, the Gas Service, afterwards renamed the Chemical Warfare Service, was made responsible early for both offensive and defensive gas warfare in the American Expeditionary Forces, the Medical Department was largely concerned with the many problems incident to the use of this new military weapon which, from its technical knowl-

edge, it alone was competent to solve. Its relationships in this connection can best be shown graphically (Chart IV). This chart indicates its activities and points of contact in this direction from beginning to end.

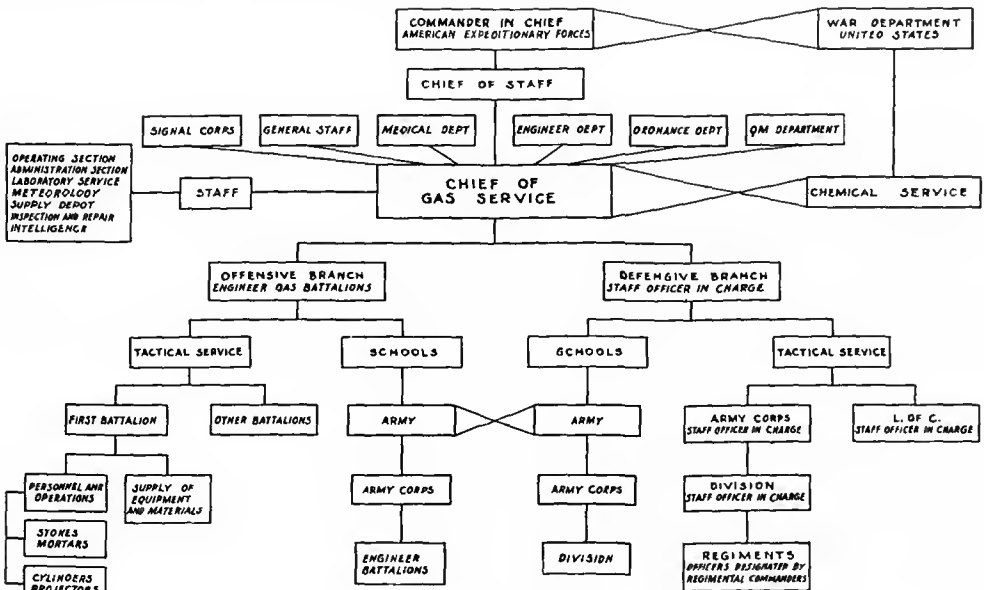


CHART III.—Gas Service organization, American Expeditionary Forces

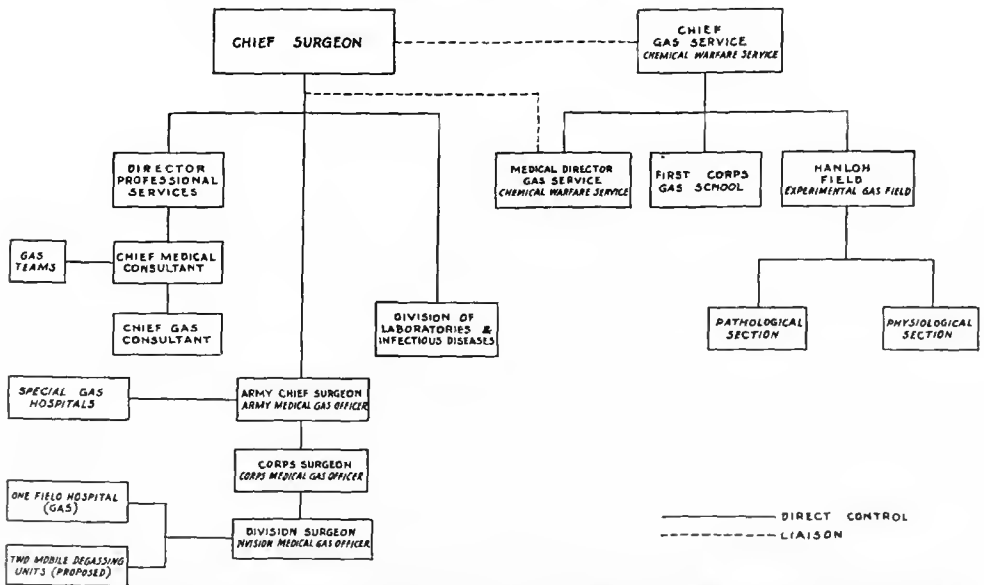


CHART IV.—The Medical Department in the organization for gas defense, training, research, and treatment, American Expeditionary Forces

Through the medical director of the Gas Service, the director of professional services, chief medical consultant, and chief gas consultant, the chief surgeon was in close touch at all times with such matters pertaining to the treatment and care of the gassed as came within the purview of the medical consultants, gas poisoning being considered a medical rather than a surgical question.

Direct contact was maintained between the division of laboratories and infectious diseases and the pathological and physiological sections of the Gas Service experimental field, generally known as Hanlon Field (q. v.). Through this division of the chief surgeon's office, American Expeditionary Forces, the Gas Service (Chemical Warfare Service) was supplied with the necessary personnel, either medical officers or officers of the Sanitary Corps, for the highly technical work along medical and allied lines, to which reference is made later, and for which the Gas Service had not the qualified personnel.

CHIEF GAS CONSULTANT

The full report of the consultant in general medicine for gas is given in Appendix, pages 826-829. Attention here need be directed only to the fact that, under his direction, the activities of the section of gas poisoning of the office of the chief medical consultant, were conducted along the lines of instruction of Medical Department personnel, treatment and hospitalization, and the actual supervision of the care of the gassed.

THE MEDICAL DIRECTOR, CHEMICAL WARFARE SERVICE

When the first medical director left the Gas Service in December, 1917, the work of the defense section was assumed by an officer of the Corps of Engineers (later of the Chemical Warfare Service).¹⁴ The second medical director, who assumed the duties of this office on December 14, 1917,¹⁵ acting in this capacity during the remainder of the war period (and longer), was not responsible for the defensive aspect of gas warfare.

At first his duties were largely concerned with the instruction of medical officers which it was deemed advisable to inaugurate as these officers arrived in constantly increasing numbers.¹⁶ (See "Instruction and training," *infra.*, p. 43.) As our participation in the actual military operations was inaugurated and our divisions began to take over sectors independently of allied control, the duties of the medical director came to be more largely concerned with inspection than with instruction. (See inspection reports of the medical director, Gas Service, Chapter IV, pp. 67-73.) In this capacity he inspected from time to time troops along the front area, hospitals, hospital trains, etc., as to methods and facilities for the care of gassed cases.

Because of the close relationship existing between the Medical Department and the Gas Service the medical director was at all times the liaison officer between these two services. He was the medical adviser to the chief of the Gas Service, and the adviser of the chief surgeon, American Expeditionary Forces, on matters relating to gas warfare. In addition to these general duties he collected for the chief of the Gas Service all physiological and medical information having any bearing on the problems of gas warfare; he supplied the chief surgeon such information as came into the hands of the chief of the Gas Service having any bearing on the medical aspects of gas warfare, especially concerning new treatment of gas casualties, combatting the effects of the enemy gases not only from a therapeutic but also from a prophylactic point of view. When the chief of the service or the chief surgeon deemed it necessary to obtain fuller information in regard to a gas attack he proceeded to the gassed sector for the purpose of investigating and obtaining all possible information concerning the attack.

When conditions warranted he called upon the director of laboratories for pathologists for special investigations, in accordance with an arrangement made by the director of the division of laboratories and infectious diseases, chief surgeon's office, with the chief of the Chemical Warfare Service.¹⁷

INSTRUCTION AND TRAINING

In Chapter I (p. 32) it has been noted that as medical officers finished the course of instruction given at the Fort Sill school for instruction in gas defense in the United States they were assigned to the various National Army and National Guard divisions, and that chemists who had been trained in gas defense at American University in Washington were detailed to these medical officers as chemical advisers.¹⁸ There were 33 medical officers and 32 chemists so trained.¹⁸ There was thus formed a nucleus for divisional medical personnel in the American Expeditionary Forces with some specialized knowledge with respect to gas warfare. How much this personnel was utilized in the American Expeditionary Forces is problematical. It will be remembered that the Engineer Corps took up this instruction in the United States in April, 1918; thereupon the medical officers who had previously been assigned as instructors were regarded as available for other duties and were so assigned. At all events, the average medical officer upon arrival in France possessed very meager knowledge of the subject of gas warfare, of the effects of gas poisoning, and of the treatment therefor. From the beginning of the arrival of our troops in France it was recognized by the Medical Department, then charged with defensive gas warfare, that steps must be taken toward furnishing the needed instruction and training of Medical Department personnel and troops to supplement such as had been given in the United States, and as might be given by the trained medical officers assigned to divisions, as noted above. Numerous reports embodying suggestions along this line were formulated by medical officers.

While throughout the Medical Department personnel received gas training through their own officers, it was only at the beginning that the Medical Department did anything in this direction, so far as the American Expeditionary Forces generally were concerned. The duty devolved on the Gas Service, later the Chemical Warfare Service.

The sources of Medical Department gas instruction in the American Expeditionary Forces were several, and it is deemed best to summarize the more important ones:

(1) From Allies: (a) Facilities furnished our medical officers even preceding our entrance into the war. (b) To our divisions with Allies as a part of instruction in general. (c) Information furnished formally to Chemical Warfare Service from time to time. (d) Information furnished more or less informally to chief surgeon, to medical director, Gas Service, and to other medical officers. (e) Through interallied conferences (Appendix, p. 812)—at the early conferences we were in the position of learners and not confrères. (f) Publications. These were freely supplied us.

(2) From our own higher authorities: (a) Numerous circulars and bulletins emanated from the offices of the chief of the Chemical Warfare Service, the chief surgeon and the medical director, Chemical Warfare Service; also some from division surgeons. The material for a part of these came from our Allies; other similar material was compiled by our medical officers.

(3) From American Red Cross: A special book containing material from our allies was distributed to our Army by the Red Cross.

(4) Personal teaching: This was given as deemed appropriate by the medical director, Chemical Warfare Service, by division surgeons, by division gas officers, and by gas consultants.

FIRST CORPS GAS SCHOOL

On October 15, 1917, the First Corps center of instruction was established at Gondrecourt.¹⁹ The gas school,^b which was part of the center, was under the direction of a medical officer, who started instruction on that date.²⁰ The program of instruction is given in the Appendix (p. 838).

INSTRUCTION OF MEDICAL PERSONNEL

By the time the second medical director assumed his duties, on December 14, 1917,¹⁵ large numbers of our medical officers were arriving in France, the majority of them with inadequate knowledge of the methods employed in the treatment of gas casualties. As previously stated, his first efforts were directed toward overcoming this state of affairs.¹⁵ Pamphlets on the medical aspects of gas warfare were distributed, and lectures were delivered to the medical officers and other personnel at hospitals and in divisions. The instruction included: ¹⁵ (1) A general explanation of the methods of chemical warfare employed by the enemy. (2) Symptomatology of gas poisoning, including a description of the lesions. (3) The diagnosis of gas poisoning. (4) Treatment. Medical officers were furnished with the latest information regarding the diagnosis and treatment of gas casualties. Some of the pamphlets of instruction which were given the widest circulation among the medical personnel may be found in the Appendix (pp. 833, 838).

COURSE OF INSTRUCTION FOR DIVISION MEDICAL GAS OFFICERS

As division medical gas officers were appointed, in accordance with authorization of August 29, 1918,²¹ each was sent to the school of pharmacy of the University of Paris (Ecole de Gaz) for a four-day course of instruction before being assigned to his respective division for duty. (See Appendix, p. 838).

SPECIAL GAS UNITS FURNISHED BY MEDICAL DEPARTMENT

OVERSEAS REPAIR UNIT

In complying with instructions ³ with respect to supplying personnel for the Gas Service, the Medical Department delegated Sanitary Corps officers and men to report to the chief of the service as required. In Chapter I reference is made to the fact that a group of specially trained men, constituting Overseas Repair Unit No. 1,²² was sent to France to repair and otherwise keep in order the gas masks and other gas-defense appliances supplied by the Medical Department. This unit was composed of 3 officers and 113 men of the Sanitary Corps, who, upon arrival in France, December 13, 1917, reported to the chief of the Gas Service and were distributed by him as he saw fit.²³

^b This gas school, referred to as the first gas school (History of Chemical Warfare Service, American Expeditionary Forces, Vol. I, 8. Copy on file, Historical Division, Army War College) was the only one of the gas schools in which the Medical Department participated.

GAS TEAMS

In May, 1918, there was transmitted to the chief surgeon a plan, formulated in the office of the chief consultant, Medical Services, providing for the establishment of two emergency gas teams in each base hospital of the American Expeditionary Forces, to be called on short notice to relieve the strain in evacuation and field hospitals in the event of sudden gas attacks.²⁴ The plan was approved by the chief surgeon, American Expeditionary Forces, on June 2, 1918, and several teams were organized accordingly, each consisting of one medical officer, especially trained, two nurses, Army Nurse Corps, and two orderlies, Hospital Corps.²⁴ On July 19, 1918, however, strenuous objection was made to the plan by the chief surgeon, First Army, in the following communication:

[3d Ind.]

CHIEF SURGEON'S OFFICE, 1ST ARMY,

July 19, 1918.

To Chief Surgeon, A. E. F., S. O. S.

Attention Col. Glennan and Col. Reynolds.

Returned.

1. On July 18th two communications re same subject, originating in office of chief consultant, Medical Services, were referred back to your office with my views on this subject.

2. It is out of the question for base hospitals to furnish gas teams unless the divisions are near the base hospitals, as is the case with the Toul and Baccarat sectors, both relatively unimportant, the proximity being accidental and not likely to occur on any other front.

3. When these installations were made, we were forced to accept the locations granted; now we take what we want, and the base hospitals will be far from the scene of battle.

4. By my verbal authority the commanding officer of the hospital group sent forward to Baccarat or Toul assistance in his ambulances, but a glance at the map will show the impracticability of this procedure on the really active front where our activities in the future will be.

5. Reference to inclosed orders to division surgeons with the two communications cited will show that one field hospital in each division has been set apart for gassed cases and additional equipment, based upon the adequacy of motor transportation, added.

6. This hospital must be as far forward as safety from direct gunfire admits, and is no place for female nurses, as there will be no accommodations.

7. Personal experience with a large number of gassed cases in the 2d Division shows conclusively that men can be trained for this particular service, and their work was so admirable I was able to evacuate over 600 cases promptly.

8. Evacuation hospitals are for battle casualties, and it is purely accidental that Evacuation No. 2 has accommodations for gassed cases, and this arrangement was dictated by the nearness of Baccarat to the trenches, an incongruity the French have recognized, as is shown by their abandonment of their own H. O. E. at that point.

9. This office has under consideration the advisability of moving Evacuation No. 2 back to Badonviller, as the drawing back of the line has placed the unit in the zone of direct fire, and only a shortage in ambulances and the relative unimportance of this sector has postponed the move.

10. The divisional consultant in medicine could perform most valuable service in training the personnel of the hospital set aside for gassed cases, and in emergency could appeal to the corps chief surgeon for assistance from a division in reserve.

11. Attention must again be invited to the propensity for basing all modifications of the sanitary service upon position warfare, which will not obtain again except in the impassable Vosges sector; and while this office welcomes the valuable suggestions of the consultant service, it is unquestionably a fact that much effort and time would be saved were inquiry made as to what was being done and how any recommendation could be coordinated to meet the constantly shifting warfare with its new problems before communications were started upon the devious channels of correspondence.

(Signed)

A. N. STARK, Colonel, M. C.

Following this objection, no further action was taken in the matter of organizing or using gas teams.

DIVISION, CORPS, AND ARMY MEDICAL GAS OFFICERS

In the brief discussion of the medical gas officers of division, corps, and army, the division is considered first, for the reason that the corps and army were not organized until after certain divisions had had gas experience, and had inaugurated medical arrangements which served later as the basis of organization for all.

Moreover, while our corps and armies had medical gas officers, they were not prescribed as was the case with divisions (Par. VIII, G. O. No. 144, G. H. Q., A. E. F., August 29, 1918) being apportioned by army and corps surgeons, respectively, and only as the need arose.

DIVISION MEDICAL GAS OFFICER ^c

The necessity for having division medical gas officers was apparent from the beginning, but the appointment of these officers was not accomplished until late in June, 1918. Our gas casualties were constantly increasing, and large numbers of men claiming to be gassed were being evacuated to the rear, where, upon examination, it was found they were not gassed. This condition resulted in much undue labor, and greatly weakened the strength of front area organizations. Inspector officers of our army reported that the rank and file were not properly instructed in medical gas matters. Reports were also made that no one in the front areas assumed charge of this important work. After these facts were clearly understood, authorization for division medical gas officers was made, on August 29, 1918.²¹ As soon as the order was published, the matter of the appointment of these officers was taken up by the chief surgeon, American Expeditionary Forces, and after the subject had been discussed with the chief medical consultant, American Expeditionary Forces, it was decided to allow each division surgeon to select the medical officer he desired as division medical gas officer. To this end, on July 8, 1918, letters were sent by the chief surgeon, American Expeditionary Forces, to all division surgeons. The following letter is one of those sent.

AMERICAN EXPEDITIONARY FORCES,
HEADQUARTERS SERVICES OF SUPPLY,
OFFICE OF THE CHIEF SURGEON,

July 8, 1918.

From: The chief surgeon, American Expeditionary Forces.

To: The division surgeon, 35th Division.

Subject: Appointment of division gas medical officers.

1. It is to be the policy in the near future to appoint division gas medical officers with each division; these officers will be assistants to the division surgeon and attached to the staff of the commanding general of the division, and their duties will be as follows:

(a) They will be the special gas medical representative in the division.

(b) They will instruct all officers and men in the symptoms and early treatment of gas poisoning.

(c) They will assume charge of the training of sanitary troops in the methods of gas treatment; instruct line officers and others in practical medical matters connected with gas warfare.

(d) They will inspect and supervise the methods of gas protection throughout the aid stations, dressing stations, and hospitals of the division and train the attached personnel in the principles and duties of handling gassed cases.

^c The data for this discussion are taken largely from the History of Chemical Warfare Service, American Expeditionary Forces, Vol. II, Part VI, Medical Director, 131 et seq. Copy on file, Historical Division, Army War College.

2. Officers detailed for this responsible work must be live, wide-awake, energetic men and must show keen appreciation of the work. Prior to assuming their duties as gas officers they will be assigned temporarily to the office of the medical director of Gas Service for special training and instruction.

3. In order to expedite this work, it is suggested that you submit to the office of the chief surgeon, as soon as possible, the name of a medical officer in your division whom you recommend for this responsible position. If possible, the officer selected should hold the grade of major, but there is no objection to a captain being selected for this position.

By direction:

(Signed) H. L. GILCHRIST,
Colonel, Medical Corps, N. A.

Owing to delays in mail, constant movement of troops, and other factors, many of these communications were not delivered, and replies in some instances were lost in transit. As a result, much delay was occasioned in the selection of these officers, but by the first week of October, 1918, a gas medical officer had been appointed in each division.²⁵

The following rules governing division medical gas officers were promulgated by the chief surgeon, American Expeditionary Forces:²⁶

1. For each division, a medical officer of the grade of major or captain will be assigned as a division medical gas officer and director of mobile degassing stations, and there will be assigned under him one sergeant and one private first class, or private, Medical Department, to be selected by the division surgeon. The medical gas officer will bear the same relation to the division surgeon as does the director of field hospitals and ambulance companies.

2. The division medical gas officer is charged especially with supervision over all gas matters in the division to which he is assigned. In this connection he will institute measures to prevent the depletion in strength in the fighting forces from avoidable errors in connection with the management of gas casualties.

He will also institute measures for—

(a) The instruction and training of sanitary troops in the best methods of handling gas cases and of the rank and file in first aid to the gassed.

(b) The establishment at advance aid stations, dressing stations, and other relief stations of an efficient system and proper equipment for the administration of first aid for the gassed.

(c) The supervision of the evacuation of all gas casualties.

(d) The supervision of the methods of gas protection throughout the aid stations, dressing stations, and hospitals of the division.

3. He will act as medical adviser to the division gas officer and will cooperate with him in every way possible.

4. He will collect and transmit to the designated Army laboratory interesting post-mortem specimens resulting from the actions of poisonous gases.

5. He will constantly be on the alert for suspicious symptoms in gassed patients which indicate the use by the enemy of new gases or new mixtures, and any signs of such will be communicated immediately through the division surgeon to the medical director of Chemical Warfare Service. The division gas officer will also be notified of such information.

6. As director of mobile degassing stations he will direct and supervise the operation of the mobile degassing units attached to his division; and to that end he will, under the direction of the division surgeon, designate the location of these units as may be necessary during or after a gas bombardment, and the closing and reassembling of them as soon as practicable.

7. He will keep the division surgeon, division gas officer, and organization commanders thoroughly informed as to the location of the degassing units and the shortest possible route leading to them.

8. His duties during the active operation of the units comprise the supervision of the bathing of those exposed to the fumes of poisonous gases; the careful examination of the men before being stripped and during the bathing period; and the immediate removal to hospitals of those showing signs of poisoning from the effects of gases.

9. His activities, therefore, cover the entire period from the time the gas attacks commence until the men participating therein have been degassed and disposed of. In order to perform these duties properly he must be thoroughly familiar with the terrain of the country occupied by the division, as well as the location of the different organizations.

10. The division medical gas officer will also inspect and report upon the administration of the degassing units; the efficiency, instruction, and adequacy of the medical personnel in gas matters; the condition of the hospitals and relief stations, in so far as they relate to the care of cases suffering from the effects of poisonous warfare gases, together with the facilities for handling them; and in general all matters affecting the care, well-being, and comfort of gas casualties.

11. At the end of every month each division medical gas officer will forward to the medical director of Chemical Warfare Service, for transmittal to the chief surgeon, American Expeditionary Forces, a report of the conditions noted by him during the month, indicating the principal medical gas defects, if any; the number of gas attacks; number of actual gas casualties reported; number returned to duty as not gassed; measures taken for the prevention of gas casualties, and other recommendations deemed necessary.

12. All literature, reports, records, etc., received by the division medical gas officer will be carefully preserved and filed and will form part of the records of that office.

Report of the course of instruction given division medical gas officers may be found in the Appendix (pp. 833, 838).

CORPS MEDICAL GAS OFFICERS

In the organization of the medical staff of the First Corps provision was made for a corps medical gas officer, whose duty it was to supervise the work of the Medical Department of the divisions of the corps in connection with the prevention and treatment of gas injuries, and to perform the same service for the corps troops.²⁷ The situation in corps generally is described under "Division, corps, and army gas officers."

ARMY MEDICAL GAS OFFICERS

In the organization of the office of the chief surgeon of the Second Army provision was made for a "medical gas treatment officer," with duties, with respect to gas, analogous to those of medical and surgical consultants.²⁸ He exercised supervision over instruction of all medical personnel in the treatment and management of cases of gas poisoning. In the First Army, from September, 1918, until the cessation of hostilities, a medical officer was designated as "director of gas hospitals." (See Appendix, p. 827, Report of the Consultant in General Medicine for Gas Poisoning, par. 6.)

GAS HOSPITALS FOR DIVISION, CORPS, AND ARMY

DIVISION GAS HOSPITALS

The use of one of the four field hospitals of the division as a gas hospital was almost universal, though it was not deemed wise to designate a particular field hospital as a gas hospital by higher authority, as this might have hampered the division surgeon concerned under some circumstances in the Second Army.

The normal distribution in a divisional area was as follows:²⁹ (1) A division in line in active offense had one field hospital as a triage for gassed. (2) In line, holding but an active offensive, one field hospital for slightly gassed and convalescents. (3) In line in a quiet sector or in training, one field hospital to meet the needs, among other circumstances, of a gas attack.

CORPS GAS HOSPITALS

A plan was proposed for allotting three mobile gas hospitals to each corps, each to have a capacity of 1,500 beds, and to be operated under the plan of an evacuation hospital.^{30 d}

⁴ This plan was not carried out; no corps gas hospitals were used at any time.—Ed.

ARMY GAS HOSPITALS

A provisional hospital for the treatment of gassed cases was established August 29, 1918. (For the full history, see Appendix, p. 840; see also Appendix, pp. 826, 827, Report of the Consultant in General Medicine for Gas Poisoning, par. 5.)

In the St. Mihiel action one gas hospital was established at the Justice hospital center at Toul and one in the French gas hospital at Rambluzin. The personnel of these hospitals was composed of casualties or of officers and men loaned from base or evacuation hospitals, ambulance companies, etc. In each hospital one officer thoroughly conversant with the principles of the care of the gassed was stationed.

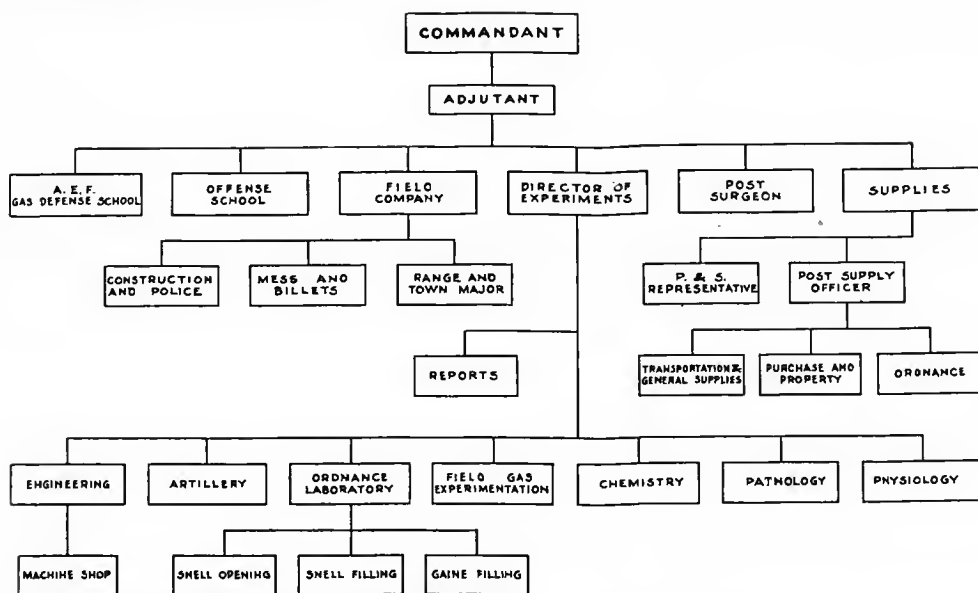


CHART V.—Organization chart of Hanlon Field (Experimental Gas Field), American Expeditionary Forces, November 23, 1918

During the Meuse-Argonne operation, five hospitals were designated by the chief surgeon to receive gassed cases. These were Rambluzin, capacity 250 beds; La Morlette, capacity 550 beds; Julvecourt, capacity 400 beds; Rarecourt, capacity 250 beds; Villers Daucourt, capacity 200 beds. The officers and personnel of these hospitals, as in the previous action, were largely casual officers and men from ambulance companies, evacuation hospitals, etc.

On October 9, 1918, the property and personnel assigned to the gas hospital was taken over by Base Hospital No. 87.³¹

RESEARCH

HANLON FIELD^e (EXPERIMENTAL FIELD, CHEMICAL WARFARE SERVICE)

It was decided, in January, 1918, to establish an experimental field for the Chemical Warfare Service (then the Gas Service). Accordingly, after an

^e The major portion of this report is included in Chapter XXI of the present volume.

investigation of sites in the vicinity of Chaumont and Langres, one was selected within 3 miles of General Headquarters, to the east of Chaumont. It was known as the Biesles range. Authorization for the requisition of an amount of ground including about 20 square miles was given by the French on March 6, 1918.³² The whole area, as finally occupied, was requisitioned by April 20, 1918. The entire organization, including the sections with which the Medical Department was directly concerned, is shown in Chart V. The commissioned personnel supplied by the Medical Department included 4 officers of the Medical Corps, 1 of the Sanitary Corps, and 4 officers of the Medical Department who were transferred to the Chemical Warfare Service.

It has been noted (p. 42) that the Medical Department supplied the personnel for the physiological and pathological sections, which, at first, operated as one section, and which rendered a combined report.^f

The name of the field was changed in August, 1918, from the experimental gas field to Hanlon Field, in honor of Second Lieut. J. T. Hanlon, of the First Gas Regiment, who was the first officer of the Chemical Warfare Service killed in action.³³

REFERENCES

- (1) Memorandum to The Adjutant General from the Surgeon General, February 17, 1915, recommending that Maj. James Robb Church, M. C., be ordered to report to the American Embassy, Paris, France, for duty as a military observer. See, 150021-N, From The Adjutant General of the Army to Maj. James Robb Church, M. C., November 15, 1915. Subject: Detail as military observer. Second indorsement from the Surgeon General to The Adjutant General, June 12, 1915, on letter from Chief of War College Division, General Staff, to the Surgeon General, June 5, 1915. Subject: Detail medical observer with French Armies. On file, Record Room, S. G. O., 150021 (old files). Letter order from The Adjutant General, to Maj. James R. Church, M. C., November 15, 1915. Subject: Detail. On file, Commissioned Personnel Division, S. G. O. Letter from The Adjutant General to Maj. S. H. Wadhams, M. C., September 25, 1916. Subject: Detail as military observer. On file, Record Room, S. G. O., 76283 (old files).
- (2) Report: "Some Notes on the Establishment of the Gas Service in the A. E. F.," by Maj. James Robb Church, M. C. Copy on file, Historical Division, S. G. O.
- (3) G. O. No. 8, G. H. Q., A. E. F., July 5, 1917.
- (4) Memorandum from the Surgeon General, U. S. Army, May 25, 1917, re Maj. James R. Church, M. C. On file, Record Room, S. G. O., 49838 (old files).
- (5) Personal Record of Maj. James R. Church, M. C. On file, Personnel Division, S. G. O.
- (6) Cablegram No. 16, par. 6, June 25, 1917, re authority to retain Dr. G. A. Hulett for gas work and that either Lieut. Col. James A. Woodruff or Col. Henry Jervy, Engineer Corps, be sent to France to organize gas service under the Chief Engineer Officer. See Appendix No. 2, p. 81, History of Chemical Warfare Service, Vol. I. Copy on file, Historical Section, Army War College. Also: Extract of cablegram No. 34, par. 4, July 9, 1917, forwarded by The Adjutant General to the Surgeon General, July 12, 1917. On file, Record Room, S. G. O., 49838 (old files).
- (7) Cablegram No. 34, par. 4, July 9, 1917. Also: Extract of cablegram No. 34, par. 4, forwarded by The Adjutant General to the Surgeon General, July 12, 1917. On file, Record Room, S. G. O., 49838 (old files). Also: Memorandum for the Chief of Staff, A. E. F., July 17, 1917, from Maj. James R. Church, M. C. On file, Historical Division, S. G. O.

^f Autopsies on gas cases were not made at the experimental field, but at base hospitals, and by pathologists of the division of laboratories and infectious diseases. It was found impracticable to secure pathologists for gas work exclusively and the arrangement mentioned was made in April, 1918, by the chief, Chemical Warfare Service, and the division of laboratories and infectious diseases.

- (8) Cablegram from The Adjutant General to Maj. Robert U. Patterson, M. C., C. O. Base Hospital No. 5, June 4, 1917. On file, Record Room, S. G. O., 158213 (old files). Also: S. O., No. 36, G. H. Q., A. E. F., July 14, 1917, par. 1 (detailing Capt. Walter M. Boothby, M. C., to G. H. Q., as assistant to the Chief of the Gas Service). On file, A. G. O., A. E. F. Records, Special Orders.
- (9) Personal reports of and correspondence concerning: Capt. W. B. Cannon, M. C., Capt. Reginald Fitz, M. C., and Maj. George W. Crile, M. C. On file, Record Room, S. G. O., Personnel Division, S. G. O., and Historical Division, S. G. O.
- (10) Letter from Adjutant General, G. H. Q., A. E. F., August 13, 1917, to Maj. James R. Church, M. C. Subject: Organization of the defensive side of chemical organization. See: History of Chemical Warfare Service, American Expeditionary Forces, Vol. II, Part II, 60. Copy on file, Historical Division, Army War College.
- (11) Cablegram (Pershing), No. 111-S, Paris, France, August 18, 1917, Par. 19, appointing Lieut. Col. Amos A. Fries, C. E., in charge of Gas and Flame Service.
- (12) Personal record of Maj. James R. Church. On file, Personnel Division, S. G. O. Also: History of Chemical Warfare Service, American Expeditionary Services, Vol. I, 6. Copy on file, Historical Division, Army War College.
- (13) G. O. No. 31, G. H. Q., A. E. F., September 3, 1917. Sect. IV, pars. 4 and 5.
- (14) History of Chemical Warfare Service, Vol. II, Part II, 26, Defense Division. Copy on file, Historical Division, Army War College.
- (15) Personal Records of Col. H. L. Gilchrist, M. C. On file, Personnel Division, S. G. O. Also: History of Chemical Warfare Service, American Expeditionary Services, Vol. I, 24. Copy on file, Historical Division, Army War College.
- (16) History of Chemical Warfare Service, American Expeditionary Forces, Vol. I, 24. Copy on file, Historical Division, Army War College.
- (17) Correspondence between Division of Laboratories and Infectious Diseases, Chief Surgeon's Office, A. E. F., and Technical Division, Gas Service, A. E. F., re Pathologists for Gas Service. On file, Historical Division, S. G. O.
- (18) Memorandum for the Chief of Staff from D. W. Ketcham, Colonel, General Staff, Acting Assistant Chief of Staff, April 6, 1918. Subject: Gas Training. On file, Chemical Warfare Service, 353.9. A. G. S. O. 3. C. W. S. $\frac{353.9}{278}A$.
- (19) G. O. No. 45, G. H. Q., A. E. F., October 8, 1917.
- (20) History of Chemical Warfare Service, American Expeditionary Forces, Vol. I, 8. Copy on file, Historical Division, Army War College. Also: Personal Record, Maj. Walter M. Boothby, M. C. On file, Personnel Division, S. G. O.
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- (22) Letter from officer in charge, Gas Defense Service, to the Surgeon General, October 5, 1917. On file, Record Room, S. G. O., 210189 (old files). Confidential Order No. 92, War Department, pars. 7 and 14, October 11, 1917. On file, Confidential Orders, Commissioned Personnel Division, S. G. O.
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- (24) Plan for Gas Teams. On file, A. G. O., World War Division, Medical Records Section (Chief Surgeon's files, 322.3284, Emergency Medical Teams).
- (25) List of Division Medical Gas Officers. History of Chemical Warfare Service, Vol. II, Part VI, Appendix 4, 157. Copy on file, Historical Division, Army War College.
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- (27) Report of Medical Department Activities, First Army Corps, by Col. J. W. Grissinger, M. C., Corps Surgeon, undated, 11. On file, Historical Division, S. G. O.
- (28) Report of the Chief Surgeon, Second Army, undated, 2. On file, Historical Division, S. G. O.
- (29) Evacuation System of a Field Army, by Col. Charles R. Reynolds, M. C. Copy on file, Historical Division, S. G. O.
- (30) History of Chemical Warfare Service, American Expeditionary Forces, Vol. II, Part VI, 147. Copy on file, Historical Division, Army War College.
- (31) Medical History of the Justice Hospital Group, Toul, France, undated, compiled under the direction of Col. Robert M. Thornburg, M. C., commanding.
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CHAPTER III

CLASSIFICATION AND METHODS OF USE OF WAR GASES

CLASSIFICATION BY PHYSIOLOGICAL ACTION

The gases used against American troops by the Central Powers may be classified according to their physiological action, as lacrymators (eye irritants and "tear gases"), sternutators (nasal irritants, "sneeze gases," "vomiting gases"), lung irritants (suffocants, respiratory irritants), and vesicants (skin irritants, escharotics).^a

The lacrymators produced temporary blindness. Liberation of small quantities of a gas of this type made it impossible to carry on without wearing a mask. These gases, while not responsible for many evacuations to the rear, harassed troops engaged in close fighting or in manipulating guns. Practically all of the long list of lacrymators had a bromine base.

The sternutator gases or nasopharyngeal irritants were nonlethal. They were capable, however, of producing extreme irritation of the nose, throat, and eyes, caused severe headache and nausea. The symptoms were comparatively short in duration, and the gases were not effective when the mask was worn. The inhalation of these gases before the application of the mask made mask wearing very uncomfortable and was apt to cause its premature removal and thus to subject the wearer to the effects of more important gases which usually accompanied or immediately followed the use of the sternutators. This type of gas usually arrived in the nature of a surprise, since it was used in high explosive shells. Because of this it was difficult for the troops to recognize immediately the presence of the gas. A good example of this type of gas is diphenylchlorarsine, which was long and extensively used at the front.

The suffocating gases were used to kill and contained the most deadly substances employed in chemical warfare. Severe edema of the lungs quickly followed their inhalation, and death from asphyxiation frequently resulted within a few hours. Gases of this character were rather quickly dissipated, however, and it was difficult for the enemy to maintain an effective concentration over a long period of time. Good mask discipline robbed these gases of most of their terror and placed heavy expense on the enemy when they were extensively used. The two gases of this group most widely employed along our front were phosgene and chloropicrin. Many combinations were made from these gases with other substances intended to assist them in their action.

Phosgene, a gas of high density, with an odor much like that of decaying hay or grain, is little, if at all, irritating to the eyes and has no irritant action on the skin. Its presence, therefore, was perceived with difficulty and men

^a The classification employed by the British medical historians (*History of the Great War, Based on Official Documents. Medical Services. Diseases of the War, Volume II, Including the Medical Aspects of Aviation and Gas Warfare, and Gas Poisoning in Tanks and Mines.* London, His Majesty's Stationery Office; 1923, p. 252) is as follows: (1) Acute lung irritants; (2) lacrymators; (3) direct poisons of the nervous system or paralysants; (4) sensory irritants of the eyes, nose, and upper respiratory passages (sternutators); vesicants. The paralyzant group (hydrocyanic acid and sulphuretted hydrogen) is not included in the classification followed in the present volume, since our troops were not subjected to these gases.

were gassed before they were aware of exposure. Chloropicrin requires a higher degree of concentration to cause a suffocative action than could readily be obtained in field use. It was frequently used in conjunction with phosgene, the enemy hoping that the prompt irritant effect of the chloropicrin would prevent the wearing of the gas mask, thus rendering the soldier an easy prey to the accompanying phosgene.

The vesicant type of gas made its appearance later than the others mentioned, but soon became the most important in gas warfare. It first came into prominence at Ypres on July 12, 1917, dichlorethylsulphide being the chemical used.¹ It was called by the French soldiers "ypérite," by the Italians "yprite," and by the British, "mustard gas." Gas-mask discipline offered ample protection to the eyes and lungs, but very important military results were obtained from skin burns which caused the evacuation of enormous numbers of casualties. The Central Powers considered dichlorethylsulphide their most pernicious gas, and the experience of the Allies certainly confirmed the opinion that it had won this place in military importance. This gas had many features which rendered it especially suitable. It was toxic in concentrations which could not be detected by the sense of smell; the person affected suffered no discomfort at the time of the exposure, and symptoms were not evident until many hours later. Mustard gas penetrated all clothing and was remarkably persistent on the earth or on foliage over which it had been scattered. These factors tended to increase its effectiveness; in addition to the physical action of the gas on the men themselves, the morale of troops was impaired.

Truly speaking, dichlorethylsulphide is not a gas, but a liquid, which slowly vaporizes, and is effective in either state. It volatilizes slowly at ordinary temperatures and dissociates only at high temperatures. This latter fact was taken advantage of in the treatment of contaminated clothing. Furthermore, it is readily oxidized by such substances as chlorine or bleaching powder, and these chemicals were used in purifying dugouts, trenches, and ground or foliage saturated with the gas.

The following toxic substances were most frequently used by the Germans in their chemical warfare: (1) Lacrymators: Benzylbromide. (2) Sternutators: Diphenylchlorarsine. (3) Lung irritants: Chlorine, phosgene, carbon oxychloride, chlormethylchlorformate, bromacetone, chloropicrin. (4) Vesicants: Dichlorethylsulphide, chlorarsines, bromoarsines.

This classification, while eminently practical and convenient, does not imply that some of the gases have no physiological action other than that of their group. This is not true. For instance, bromacetone and chloropicrin, when employed in concentrations too low to affect the lungs, are lacrymators.

In addition to the four groups mentioned, gas officers occasionally reported the use of substances which possessed some of the properties of both the suffocative and vesicant gases. The usual shell filling which produced this result was made of equal parts of ethyldichlorarsine and dichlormethylether. This combination caused a vesicant action of an important nature, if kept in contact with the skin, with the air excluded; under ordinary battle conditions, however, this seldom happened. These gases possessed the properties of the suffocative type to a greater degree though not so effective as phosgene and chloropicrin. Innumerable combinations of gases were encountered occasionally.

A complete list, in so far as is known, of the gases used by the enemy, includes the following: ² Acrolein, allylisothiocyanate, arsenic trichloride, arsine, bromacetone, bromoacetic ether, bromethylmethylketone, bromide of benzyl, bromide of xylyl, bromide of toluyl, bromine, carbon monoxide, carbonyl chloride (phosgene), chloroacetone, chlorine, chloropierin, cyanogen, dichlorethylsulphide (mustard gas), dichlormethylether, dimethylsulphate, diphenylchlorarsine, diphenylfluorarsine, ethyldichlorarsine, formaldehyde, hydrocyanic acid, hydrosulphuric acid, iodacetic ether, iodacetone, methylchlorsulphonic acid, monochlormethylechloroformate (palite), nitrogen peroxide, phenylcarbylamine chloride, phosphine, phosphorus trichloride, sulphur dioxide, sulphur trioxide, and trichlormethylechloroformate (diphosgene or superpalite).

METHODS OF USE

The first gases used by Germany during the war were liberated from charged cylinders secretly installed in their trenches,³ the success of such a gas attack depending upon a favorable wind which would carry the gas in high concentration slowly over the trenches of the unprotected allied troops. There is no record of the American Army having been exposed to any of the original types of cloud gas attacks from such cylinders.

This method was superseded by the projector attack and trench-mortar firing of gas projectiles.⁴ Projectors, during most of the war, were large, smooth-bore cylinders. They were built to receive large drums or bombs of about 18 c. m. diameter. Charges of explosives were put in the bottom of these cylinders and the bomb placed on top. The cylinders were placed in batteries of from six to nine and operated at an angle of 45° in a trench or in some special area that offered protection. Such a plant usually contained from 200 to 800 projectiles, and the batteries were fired by electricity. This permitted the simultaneous discharge of a vast amount of gas on a relatively small target at a range of from 1,000 to 1,500 meters. The gases so used were of the lung irritant type. A successful projector attack produced very serious results, and it could be carried out without much regard to wind direction and velocity. These bombs contained 50 per cent of their total weight in gas, as against 10 per cent in a gas shell. The great advantages were the cheap guns for the delivery of the gas and the enormous sudden concentration of the gas in a small area. Nevertheless, this method of using gas at a relatively short range necessitated great secrecy in installing the projector during the night and in getting off the attack before the allied air service located the line of projectors, else allied artillery would destroy the plant and liberate the gas among the enemy's own troops. Furthermore, the flash and noise produced usually gave the troops sufficient warning to put on masks. This method, at best, was limited to local uses and, although continued throughout the war, it became less and less frequent. During the late months of the war the enemy made an effort to improve this method by building rifled cylinders and giving the bomb more of a shell contour.⁴ This gave a slightly increased range, but did not greatly enlarge the scope of its usefulness.

Hand grenades were employed for delivering gas under certain conditions, but their use was so limited for this purpose that they did not account for many casualties.⁴

These methods all proved of relatively little importance, however, as soon as the enemy discovered that gas could be better distributed by shells.

The innovation which placed gas warfare on a very important military plane was the building of the gas shell and the distribution of these shells by the use of artillery.⁵ When first employed by the enemy the shells carried only lacrymator substances. Lethal gases made their appearance in shell about the time of the first battle of the Somme, and this method of gas warfare rapidly developed until, at the close of the war, all types of gases were being used in gas shells, with many of them as a part of the filling in high-explosive shells. Distribution of gas in this manner on a given target was limited only by the number of guns available and the rapidity of their fire. This method of delivering gas was in very small degree limited by weather conditions and had the advantage of long range. It sometimes affected the territory even beyond the actual range of the artillery, since with a favorable wind a harmful concentration of gas would float with the air currents well beyond the point of shell burst. Definite tactics were evolved with this use of gas, placing its employment on as definite a plane as were the tactical methods of other arms of the service. After the use of gas shells had been instituted, it was difficult for the troops attacked to determine during a bombardment whether only high explosives were being used or whether a gas attack as well had been launched. For this reason it compelled the wearing of gas masks by the troops as soon as they were subjected to an artillery attack, and this in itself greatly lessened their fighting efficiency.

Their shell were classified by the enemy as pure gas shell and high-explosive gas shell. The pure gas projectile was employed for its lethal and casualty-producing effect by gas alone, since the effect of detonation and fragmentation was very slight. Such shell, when filled with a lung-irritant gas, were marked with a green cross. Various combinations of these fillings were marked green cross 1, green cross 2, or green cross 3, according to the nature of the particular mixture in use. Commonly the suffocative types of shell fillings were referred to as green cross ammunition.⁶

Pure gas shells containing dichlorethylsulphide were marked with a yellow cross, and sometimes less important vesicant types received a further mark of identification such as yellow cross 1. This was later changed to green cross 3, the filling then being ethyldichlorarsine and dichlormethylether, the mixture previously described. Gas shell containing lacrymators were indicated by lettering such as "T-Stoff," "K-Stoff," "C-Stoff," and "B-Stoff."⁷

High-explosive gas shell usually contained the nasal irritants such as diphenylethylarsine and were marked with a blue cross.⁸ There is reason to believe that very late in the war some mustard gas may have been fired in high-explosive shell. The blue cross shell not only produced a gas effect but also detonation and fragmentation to a marked degree. The amount of gas filling in such a shell was necessarily small, the enemy entertaining the hope that the accompanying high explosive would assist in propelling, vaporizing, and concealing the gas. The burst of this shell, unlike the pure gas shell, could not easily be differentiated from the ordinary high-explosive shell burst.⁸

The enemy found the markings mentioned necessary to make it easy for the storage and for artillery troops which handled such ammunition and served the guns. Fortunately, the relationship of these marks to the shell contents

soon became known to the Allies. This proved of great value in quickly identifying the nature of gases employed in an attack, since unexploded shell or fragments of shell bearing these marks were found.

Among the tactical programs adopted by the enemy for the use of war gases under different conditions the following are examples:⁹

I. Counter battery fire and long-range fire (calibers, 77 mm., 105 mm., 150 mm., howitzers, 10 cm. guns):

	Per cent
Explosive shell.....	20
Blue cross gas shell.....	70
Green cross gas shell.....	10

The 15 cm. guns constituting part of the long-range group were provided with high-explosive shell only. The rate of fire during the preparation for the attack for the 77 mm. guns was found to be one shot per minute per gun.

II. Fire against infantry—creeping barrage (calibers, 77 mm., 105 mm., 150 mm., howitzers):

	Per cent
Explosive shell.....	60
Blue cross gas shell.....	30
Green cross gas shell.....	10

The 210 mm. howitzers were provided with high-explosive shell only.

III. Fire against infantry—box barrage (calibers, 77 mm., 105 mm., and 10 cm. guns):

	Per cent
Explosive shell.....	30
Blue cross gas shell.....	60
Green cross gas shell.....	10

Yellow cross gas does not appear in these orders, since the enemy never attacked immediately through an area that they had shelled with mustard gas.

Allied troops at points selected for attack by the enemy and the artillery supporting such allied troops were subjected, before the enemy infantry advance, to a gas attack with high-explosive shell containing blue cross substances, and this fire was immediately followed by green cross shell. Late in the war it very frequently happened that all areas lateral to the point of attack were neutralized by a saturating fire of yellow cross shell. Reserve troop concentrations in the rear of such points of attack, villages near the scene, roads, wooded areas, ravines, reverse slopes, and other strong points, not intended to be occupied by the enemy were also shelled with mustard gas. In some instances, when an enemy attack failed and an orderly retreat could be made, he used mustard gas to assist in covering the retreat.¹⁰

Thus it can be seen to what extent gas could be used in open warfare and how extremely difficult it was for the medical officer to determine whether one gas or a combination of gases produced the casualties he was called upon to care for. The individual patient might have been exposed to all the gases used in such an operation, or, on the other hand, he might have been in a spot where there was a significant concentration of only one of the gases.

The persistent and insidious character of mustard gas made it effective for several days after the burst of the shell. It made a good weapon, therefore, against wooded areas, billeting spaces, roads, artillery and machine-gun positions, as well as all points of cover. According to the needs of the situation, yellow cross shell could be used for surprise burst of fire, for saturation shoots, or for the area shoot. The last method, when used against inexperienced troops, was apt to cause them to minimize the danger of such concentration.

This method of fire consisted in maintaining a low concentration of mustard vapor in a given locality by slow intermittent shooting directed at that area. Such regions would be fired on frequently enough to keep up a low vapor concentration for days and weeks at a time. The inconspicuous way in which these areas were planted and kept planted with mustard gas resulted in many casualties. Directions for such area shooting are known in one instance to have been as follows:⁹

Seventy-seven millimeter guns; 100 rounds per hectare (approximately 2½ acres):

Target at 1,000 meters, 100 rounds.

Target at 5,000 meters, 125 rounds.

Target at 6,000 meters, 125 rounds.

Target at 7,000 meters, 150 rounds.

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CHAPTER IV

FIELD ARRANGEMENTS FOR GAS DEFENSE AND THE CARE OF GAS CASUALTIES

The officers particularly concerned in administrative details for gas defense from the Medical Department standpoint and in treating gas casualties were the medical director Chemical Warfare Service, the chief gas consultant, the division surgeons, and the division medical gas officers. The subjects of the present chapter can best be described in their own words. In order to accomplish this the more important reports of the officers in question are quoted more or less in full. Selection has necessarily been exercised in respect to the inspection reports of the medical director and to the reports of the division surgeons and division medical gas officers, only typical reports having been chosen for publication. In addition to those mentioned, the report of the Medical Gas Warfare Board appears here. The report of the 42d Division and that of the Medical Gas Warfare Board include supply tables. Another supply table, however, was actually in effect for a large part of the time during which we participated actively in the war. This appears at the end of this chapter in the report of a medical officer who acted as a representative of the chief surgeon at General Headquarters, American Expeditionary Forces.

ACTIVITIES OF OFFICE OF MEDICAL DIRECTOR

HISTORY OF THE OFFICE OF THE MEDICAL DIRECTOR, CHEMICAL WARFARE SERVICE, AMERICAN EXPEDITIONARY FORCES, FRANCE

I. INTRODUCTION

Col. J. R. Church, Medical Corps, reported for duty to the chief of Gas Service on August 22, 1917, to become medical director of the Gas Service. Prior to his reporting for duty with the Gas Service, Colonel Church (then major) had submitted to the chief of staff American Expeditionary Forces, on July 26, 1917, a suggested organization for a Gas Service. He remained on duty with the Gas Service until December 14, 1917, when he was relieved by Lieut. Col. H. L. Gilchrist, Medical Corps (later colonel).

Prior to receiving orders, the following telegram was received by Lieutenant Colonel Gilchrist from the office of the chief surgeon, American Expeditionary Forces:

Lieut. Col. H. L. Gilchrist, commanding officer, No. 9 General Hospital. Orders issued to-day assigning you to the Gas Service at the headquarters. Get all information possible in regard to defensive gas work before your orders arrive and before reporting for duty. Acknowledge. (Signed.) Bradley.

In view of the above, Lieutenant Colonel Gilchrist spent several days at the British gas school at Rouen, France, studying defensive gas measures, etc., in connection with the contemplated work.

* * * * *

The first few weeks were devoted to a careful study of the situation; and after surveying the entire field from a medical point of view, it was decided that the matter of greatest importance, and the one requiring immediate attention, was the establishment of a medical gas instruction campaign for the purpose of instructing medical officers in the medical aspects of gas warfare.

* * * * *

The instruction included the following:

1. A general explanation of the methods of chemical warfare employed by the enemy.
2. Symptomatology of gas poisoning, including a description of lesions caused thereby.
3. The diagnosis of gas poisoning.
4. Treatment.

With these objects in view, a hurriedly prepared article, entitled "Symptomatology, pathology, and general treatment of gas cases," was published by Lieutenant Colonel Gilchrist and distributed to the medical officers of the American Expeditionary Forces. This was the first article of the kind on the subject published in the American Expeditionary Forces, and appeared on February 8, 1918. Following the publication and distribution of this article, many others were published from time to time in the form of bulletins, in order to keep medical officers of the American Expeditionary Forces conversant with the latest developments in medical gas matters.

III. LECTURES

The medical director visited most of the divisions and many of the hospitals, and lectured to the officers and other personnel on the subject of warfare gases from a medical point of view, laying special stress on the subjects of prevention and treatment. Before the medical consultant board was organized in the American Expeditionary Forces, the only instruction promulgated along these lines was that given out from the office of the medical director of the Gas Service.

IV. PRELIMINARY WORK

Shortly after the medical director reported for duty, an attempt was made to incorporate into the Gas Service a medical division, as one of the departments of this service. In the plan of organization suggested, it was contemplated to have specially trained medical officers with all divisions as division medical gas officers, to act under the medical director of the Gas Service. All medical gas research and laboratory work was to be under this division. The medical division was to be in close liaison with the Medical Department of the American Expeditionary Forces. This plan, however, was disapproved in the general organization of the Gas Service.

After the 42d Division had been subjected to several gas attacks which resulted in a considerable number of casualties, the division surgeon succeeded in having a division medical gas officer appointed by order of the division commander. Fortunately, one of the medical officers in the command, Capt. Jasper Coughlan, had received instruction in medical gas matters in the States, and had given the subject much study. He was appointed division medical gas officer and organized a thorough and systematic method for handling gas cases in the division. This plan proved highly successful.

V. DIVISION MEDICAL GAS OFFICERS

The necessity for having division medical officers was apparent from the beginning * * *. Our gas casualties were constantly increasing; and large numbers of men claiming to be gassed were being evacuated to the rear, where, upon examination, it was found that they were not gassed. This condition resulted in much undue labor and greatly weakened the strength of front-area organizations.

Inspectors general reported that the rank and file were not properly instructed in medical gas matters. Reports were also made that no one in the front areas assumed charge of this important work. After these facts were clearly understood, authorization for division medical gas officers was made, by Paragraph VIII, General Order 144, General Headquarters, American Expeditionary Forces, dated August 29, 1918. As soon as the order was published, the matter of the appointment of these officers was taken up; and after the subject had been discussed with the chief medical consultant of the American Expeditionary Forces, it was decided to allow each division surgeon to select the medical officer he desired as division medical gas officer. [See Chap. II, p. 46.]

* * * * *

Due to delays in the mail, constant movement of troops, etc., many of these communications were not delivered, and replies in some cases were lost in transit. As a result, much delay was occasioned in the selection of these officers. However, by the first week of October, 1918, the division medical gas officers had all been appointed. * * *

VI. COURSE FOR DIVISION MEDICAL GAS OFFICERS

The next matter of importance to be considered was the instruction of these officers. Because the nature of the work was entirely new, it was decided to give them a special course of training before assigning them to their new duties. This course, which was conducted very successfully, was given in Paris, and lasted four days, commencing October 7, 1918. [See Appendix, p. S38.]

VII. PORTABLE TUNNELS FOR NEUTRALIZATION OF MUSTARD GAS CASES

In January, 1918, the French reported that they were neutralizing mustard gas clothing by the use of chlorine. Based on this, the medical director made recommendation to the chief, Gas Service, that portable tunnels be constructed and mounted on trucks, and that, following mustard gas attacks, they be rushed to the sector involved and there erected. Those exposed to the fumes of mustard gas would then be compelled to apply their respirators and to enter the tunnel, into which was to be thrown a strong concentration of chlorine gas. This plan was approved by the chief of Gas Service, and the tunnels were erected under the direction of the medical director. This method was presented to the Interallied Gas Conference which met in March, 1918. The tunnels, however, were never put to use in the field.

VIII. DEGASSING STATIONS

In view of the importance of early bathing in connection with the treatment of men exposed to the fumes of mustard gas, and the fact that bathing facilities were scarce along large sections of the front occupied by our forces, plans and specifications of a motorized mobile degassing plant were prepared by the medical director and later approved by the general staff and authorized by Paragraph VIII, General Order 144, General Headquarters American Expeditionary Forces, dated August 29, 1918. Two of these plants were authorized for each division.^a [See Fig. 1.]

Description of motorized degassing stations.—The degassing station, devised by Col. H. L. Gilchrist, Medical Corps, medical director of Chemical Warfare Service, American Expeditionary Forces, constructed under authority of memorandum from A. C. of S., G-4, G. H. Q., A. E. F., June 2, 1918, and successfully tried out on July 24, consists of the following:

(a) One motorized tank car capable of carrying 1,200 gallons of water with rotary pump attachment for filling the tank and Stanley heating device attached at the rear end for heating the water and generating the steam.

Twenty-four shower heads, each capable of ejecting 4 quarts of water per minute, attached to 1½-inch tubing and arranged in three independent section frames, each containing eight shower heads. These section frames are 10 feet long and 30 inches wide, with independent valves. The sections are connected together by means of 2-inch tubing 10 feet long, to which is attached the hose leading from the heater. The shower heads are supported on a portable iron frame made from 2-inch tubing with sliding joints. The frame, erected, is 7 feet 6 inches high. Different lengths of hose are carried for the purpose of connecting the heating device with the showers.

All the above equipment is carried on the tank car, thus rendering it an independent bathing unit in itself.

(b) One 3-ton truck of standard make for transporting clothing and equipment.

(c) One motorcycle with side car attachment for the commanding officer.

(d) One 50-foot ward tent with uprights and pins for furnishing cover.

The above station is intended for use only where no available water is at hand. At places where water can be found the tank car with water is replaced by a smaller car equipped with the same heating device, suction pump, showers, etc. With this equipment the water is pumped directly through the heating device into the showers. Equipments *b*, *c*, and *d* are the same with both stations.

Objects of degassing stations.—These stations are intended to give hot baths and clean clothing to those subjected to the fumes of mustard gas at the nearest possible points to where gas bombardments take place.

Distribution of degassing stations.—Two of these degassing stations are assigned to each division when in the front area.

Control of the degassing stations.—The degassing stations, when assigned to a division, are under direct control of the chief surgeon of the division, who dispatches them to the places where most needed.

Responsibility for the administration of the degassing stations.—The commanding officers of the degassing stations are held directly responsible for their administration, both at the base and when in action.

Departments of the mobile degassing stations.—The mobile degassing stations are divided into sections, as follows:

^a Only one experimental plant was constructed before the armistice and this was not actually employed in combat.—Ed.

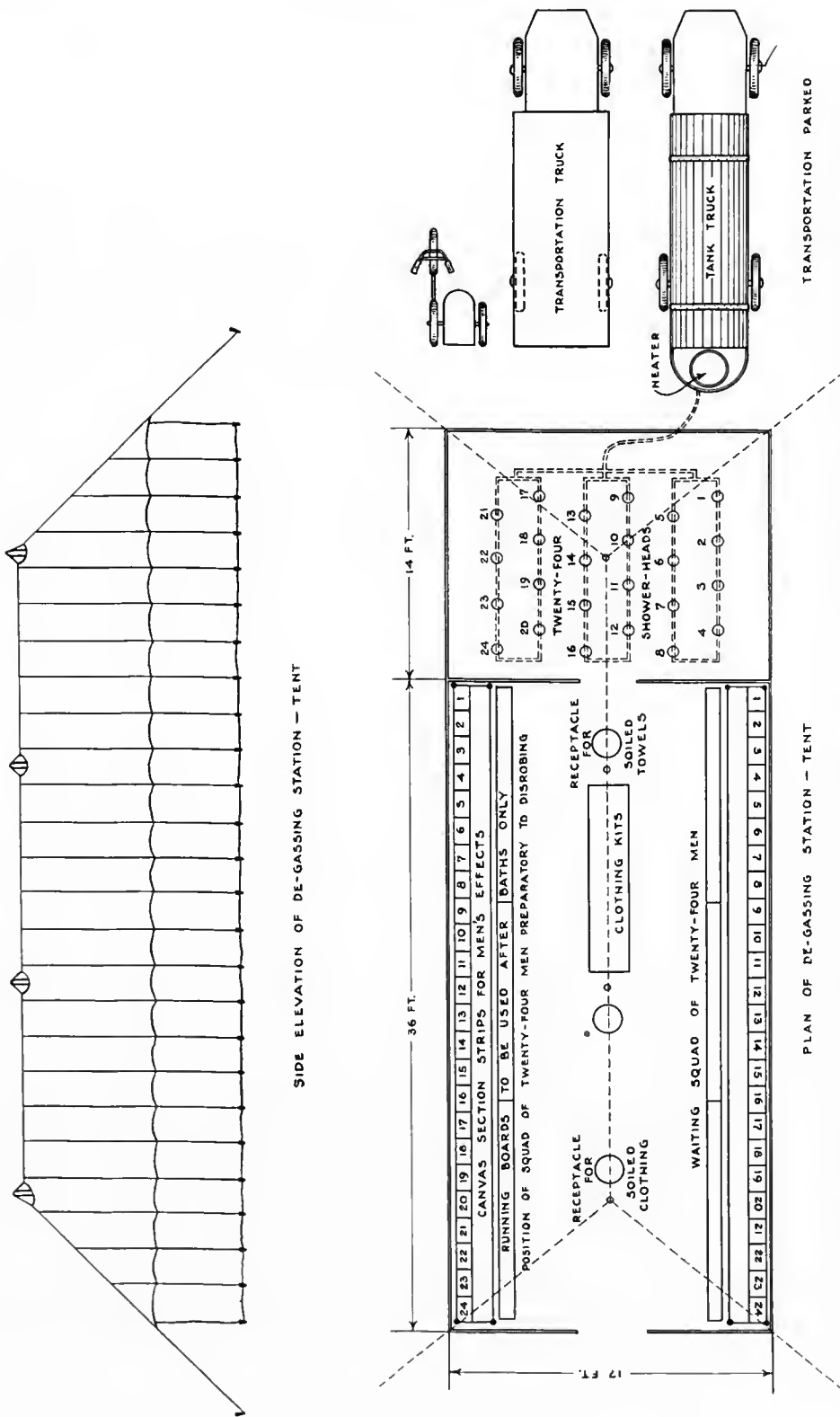


FIG. 1.—Plan of mobile degassing station, American Expeditionary Forces, designed by Col. H. L. Gilchrist, Medical Corps U. S. A., Medical Director, Gas Service, June, 1918.
Note—Tent erected only in case other shelter is not available

- (a) Reception department for the receiving of all men to be bathed.
- (b) Bathing and irrigation department.
- (c) Clothing and evacuation department.

Advantages of degassing stations.—The particular advantages of degassing stations are as follows:

- (a) Being mobile, they can be taken to the men, instead of compelling the men to march to a fixed bathing point.
- (b) Hot baths can be given to men when most needed.
- (c) They are so arranged that bathing places can be erected in a few minutes in abandoned houses or in the open.
- (d) They can be used not only for degassing men subjected to the fumes of mustard gas, but also for bathing men infected with lice and vermin and for bathing medical and surgical casualties, at the front.

Operation.—With the degassing station 24 men can be bathed in one minute and a half, and if water supply is at hand there is no limit to the number of men that can be bathed. If no water is available in the vicinity, 700 men can be bathed with that transported on the tank car. (In trying out this establishment with untrained men it required 17 minutes to pitch the tent, arrange the interior, and start the baths. The plant was dismantled in 9 minutes. Establishing the plant without the tent required 2 minutes.)

Organization and distribution of personnel of mobile degassing stations.—

- 1 captain or first lieutenant, Sanitary Corps, general supervision, reports, records, and returns.
- 1 sergeant first class, Medical Department, in general charge of records and clothing.
- 1 sergeant, Medical Department, in charge of bathing section.
- 1 sergeant, Medical Department, chief chauffeur and mechanic.
- 7 privates first class, or privates, Medical Department.
- 1 private first class to be chauffeur.

Method of employment of degassing stations.—When these units are used for degassing patients, the following plan is carried out:

All men reporting to the station are carefully scrutinized for signs of gas poisoning. Those presenting gas symptoms are treated immediately and evacuated. The others are divided into sections of 24 men each, for bathing. The members of these sections then stack arms, remove all loose equipment, and lay it on the ground in front of them. They then proceed to the lime box, where their hands are disinfected with dry lime. The same method is used for disinfecting their shoes. Blouses are then removed and disposed of according to directions, after which they proceed to the tent and stand in front of their designated numbers on the canvas, where they are instructed in the manner of taking baths. Prior to entering the tent they dip their helmets in a tank of lime water for the purpose of disinfection.

Method employed in disrobing.—In disrobing, the following plan will be adhered to:

- (a) The helmets are placed on the numbered canvas sections in front of the men and used as a receptacle for holding valuables, small trinkets, etc.
- (b) Their flannel shirts are removed and disposed of according to directions.
- (c) Shoes and socks are removed and placed with the other equipment in front of the men.
- (d) The underclothing is removed and placed in the proper receptacles.

When men are disrobing, they do not sit down, but remain standing, thus avoiding all possibility of infecting the places which are to be used when rearranging their clothing.

After all members of the squad are disrobed and their clothing and equipment have been properly disposed of, they march in column of files to the bathing department, where each man takes his place under a shower head. Before the showers are turned on, the men spray themselves with liquid soap. At a given time the showers are turned on, and 15 seconds are allowed for wetting the body. When time is a factor, three-fourths of a minute will be allowed for scrubbing the body, following which the showers will again be turned on for 30 seconds. After the bath clean towels are issued, and after their use they are placed in proper receptacles. Passing from the showers, the men's eyes, noses, and throats are sprayed with a solution of bicarbonate of soda, 5 per cent strength. They then proceed to the clothing and evacuation department, where each man is issued a clothing kit. The men then return to their places and readjust their clothing.

During the time the men are stripped they are again examined by the commanding officer and, if possible, by a medical officer for signs of gas poisoning. Those exhibiting genuine signs are immediately evacuated to the hospital. After the men have dressed themselves they return to their command.

In order to avoid delays, sections of 24 men must be ready to proceed to the baths as soon as they are vacated.

Designation.—The degassing stations are designated during the daytime by the displaying of a large blue flag and at night by a blue lantern.

Equipment.—The equipment consists of two parts:

1. An extra supply of clothing and the necessary equipment for the personnel at the base station, which is moved only when the unit changes station.
2. The equipment actually necessary when the station is erected at the front; this equipment is carried on the truck.

The amount of clothing at each degassing base station is in proportion to the number of men in the division. According to recent experience 5 per cent of the total number of men will be exposed to poisonous gases, and clothing should be provided for this number at the beginning. New phases of gas situation may cause an alteration of these figures from time to time. Of this amount, 500 complete suits or uniforms should be carried with the stations, and the remainder should be stored at the unit base station, ready for emergency use.

(1) Clothing carried with station:

- 500 blouses, assorted sizes.
- 500 breeches, assorted sizes.
- 500 flannel shirts, assorted sizes.
- 500 undershirts, assorted sizes.
- 500 underdrawers, assorted sizes.
- 500 pairs puttees (woolen leggings).
- 500 towels, hand.

The above clothing carried in gas-proof bags.

(When overcoats are worn, this article will be added to the clothing kit. No new issues of helmets, belts, socks, and shoes are made at the degassing stations.)

(2) Equipment carried with station: 1 ambulance guidon on lance staff; 1 flag (blue); 4 ax heads; 6 ax helvies; 4 spades (secured to truck); 6 lanterns (two with blue globes); 3 pick axes, with helvies; 3 buckets, galvanized iron; 4 litters, with slings; 1 hospital ward tent; 1 portable shower apparatus with 24 shower heads; 2 vermorel sprayers; 2 barrels of lime; 4 small oxygen tanks; 4 Haldane masks; 1 bag, water, sterilizing; 4 cans, galvanized iron; 1 box soap, 1-ounce cakes; bicarbonate of soda.

IX. INSTRUCTION OF PERSONNEL FOR MOBILE DEGASSING STATIONS

In order to have a sufficient number of trained officers and enlisted men for duty with the degassing stations, a school of instruction was established at a large château near Vouvray (Indre et Loire). The school was placed under the command of First Lieut. Herbert D. Snyder, Medical Corps. Only men having special training in motors, steam fitting, plumbing, etc., were selected for the work.

X. MEDICAL GAS WARFARE BOARD

On October 18, 1918, a special board to be known as the Medical Gas Warfare Board was organized under provisions of paragraph 128, Special Orders, 291, General Headquarters, American Expeditionary Forces. The composition of this board was: Col. H. L. Gilchrist, Medical Corps; Lieut. Col. H. H. M. Lyle, Medical Corps; Maj. Richard Dexter, Medical Corps; Capt. Jasper Coughlan, Medical Corps.

The duties of this board were to consider all medical gas matters. The board held its first meeting November 5, 1918, at Headquarters, First Army, and considered several matters referred to it by the chief surgeon, American Expeditionary Forces. * * * [See Appendix, p. 829.]

XIII. STERILIZATION OF CLOTHING OF GASED PATIENTS

Proper provision for sterilization of clothing and equipment of gas casualties is a serious proposition, and to that end it is believed that the only feasible method is the use of the steam sterilizer. In places where the mobile degassing unit can not be assigned to the hos-

pital, a portable water heater with shower heads can be attached to the steam sterilizer and will meet most requirements. With this apparatus 100 cases may be bathed in one hour with approximately 1 gallon of water to each man.

* * * * *

XVI. HYPERSENSITIVENESS OF SOME TO MUSTARD GAS

In investigating gas attacks it has been apparent that many men go through mustard gas attacks and suffer severe skin infections or burns, while others subjected to the same attacks under like conditions escape. The conditions may be likened to those produced by poison ivy; while some are highly hypersensitive and suffer from it, the majority of the persons escape from the poison with no apparent bad effects.

It has also been observed that those with fair skin suffer greatest from the direct action of the fumes.

XVII. LONG HAIR IN RELATION TO EYE AND RESPIRATORY TROUBLES

In examining large groups of mustard gas cases it was noted, with few exceptions, that those cases having severe eye lesions and lung irritation had long, shaggy hair on their heads. As a result, an investigation was made by several medical officers, and it was definitely decided that long hair harbored the fumes of the gas and was directly responsible to a great degree for the severity of the conditions.

XVIII. SELF-INFLICTED GAS BURNS

After a careful study of the question of self-inflicted gas burns, it is believed that many casualties entering the hospitals with severe eye lesions infect different parts of the body with fingers contaminated by discharge from the eyes.

XIX. MALINGERING

The question of malingering was introduced early in the year. There can be no doubt, because of the excessively high casualty list and low mortality, that a large number of gas casualties heretofore reported were not actually gassed. The British and French show that their mortality from gas casualties runs from 3 to 4 per cent. In our armies it is less than 2 per cent (to be exact, 1.7 per cent). This condition is not believed to be due to any better treatment received in our hands than that given by our Allies, but due wholly to the fact that a large number of reported gas casualties were suffering from other causes.

In this connection attention is invited to a report of one field hospital in which 281 men were being treated as gas casualties. Due to the utter lack of symptoms in the majority of these cases, the commanding officer of the hospital asked for a board of medical officers to examine the cases. The report of this board showed that but 90 of the 281 cases were suffering from gas poisoning, and as a result the others were returned to duty. Numerous similar reports have been received from other sources. There is no doubt that many men have claimed they were gassed in order to get out of the front lines; that a still larger number thought they were gassed and were suffering from conditions which might be called gas mania; and that others smelled the odor produced by the explosions of ordinary shell and became panie-stricken in the belief that they were gassed. In view of the low mortality mentioned above, it is believed, if the true facts were known concerning our gas casualties, that they would not be over one-third those actually reported.

XX. PERSONNEL OF OFFICE OF MEDICAL DIRECTOR

Commissioned:

Col. H. L. Gilchrist, Medical Corps, medical director, from December 14, 1917, to November 25, 1918.

Maj. Richard Dexter, Medical Corps, assistant to medical director, from March 11, 1918, to June 7, 1918.

First Lieut. George W. Perry, Sanitary Corps, assistant, from July 16, 1918, to August 16, 1918.

First Lieut. Herbert D. Snyder, Medical Corps, assistant, from October 15, to November 25, 1918.

Enlisted:

Corpl. H. M. Valley, Medical Department, stenographer and in charge of office records, etc., from June 25, 1918, to November 25, 1918.

APPENDIX No. I^b

[Copy of memorandum submitted by Lieutenant Colonel Gilchrist to chief surgeon, American Expeditionary Forces, suggesting duties of medical director, Gas Service, and plan of organization of the Medical Corps for handling gas casualties.]

MEDICAL DIRECTOR OF THE GAS SERVICE

Owing to the importance of medical gas warfare measures, a specially trained medical officer will be appointed by the commanding general, American Expeditionary Forces, upon the recommendation of the chief surgeon, American Expeditionary Forces, to be known as the director of medical gas warfare, American Expeditionary Forces, who will be charged with the organization and control, under the direction of the chief surgeon, of these different measures.

In view of the close relationship existing between the Medical Department and the Gas Service, American Expeditionary Forces, in connection with the subject of gas warfare, he will, for purposes of coordination, be assigned to duty with the Gas Service as its medical representative. He will act as the liaison officer between these two services and with the medical gas services of our Allies. All transactions between the services will be conducted through this officer.

The director of medical gas warfare will be the medical adviser of the chief of Gas Service and the gas adviser of the chief surgeon of the American Expeditionary Forces. Besides the duties already specified, he will collect for the chief of the Gas Service, American Expeditionary Forces, all physiological and medical information having any bearing on the problems of gas warfare; he will supply the chief surgeon such information as comes into the hands of the chief of Gas Service which has any bearing on the medical aspects of gas warfare, especially concerning new treatment of gas casualties, with reference to combatting the effects of the enemy gas, not only from a therapeutic, but also from a prophylactic point of view. To this end the chief of Gas Service will supply the medical director all information concerning gas warfare which has any bearing on medical matters.

He will prepare for publication and distribution to medical officers and others, extracts from reports pertaining to medical gas matters sent to the gas service of chief surgeon. All expenses in connection with such publications will be borne by the Medical Department.

He will be prepared to lecture to medical officers and others on the subject of gas poisoning. He will cooperate in every way possible with the chief consultant, medical services, American Expeditionary Forces, and keep him thoroughly acquainted with all new or suspicious symptoms following gas attacks.

He will arrange for direct telephonic or telegraphic intercourse with the division medical gas officers and others, whereby the chief surgeon and the chief of gas service can be notified immediately following gas attacks.

He will inspect, from time to time, troops in the front area, hospitals, hospital trains, etc., as to methods and facilities for the care of gassed cases.

When the chief of gas service or the chief surgeon deems it necessary to obtain fuller information in regard to a gas attack, the medical director will proceed to the gassed sector for the purpose of obtaining all possible information concerning the attack. Being a member of the gas service, he will represent the chief of Gas Service in his interview with gas officers. Being a medical officer, he will represent the chief surgeon, American Expeditionary Forces, in his transactions with medical officers; and, when necessary, he will examine carefully the casualties.

When conditions warrant, he will call upon the director of laboratories for a pathologist, to proceed to the designated place for duty in connection with special investigations. Copies of reports from the pathologists immediately following such visits will be submitted directly to the medical director of the gas service, who will incorporate them with the general report of the gas attack to be made to the chief of gas service, a copy of which will be furnished to the chief surgeon.

During the investigations the medical director will cooperate from a medical standpoint with the personnel of the gas service in the study of any clinical manifestations which may suggest the employment of new gases, and in the investigation of their effects.

^b See p. 153, Vol. II, History of Chemical Warfare Service, American Expeditionary Forces.

Any important information obtained by the medical director during these investigations will be communicated immediately to the chief of Gas Service and the chief surgeon of the American Expeditionary Forces by telephone or telegraph; a full written report will follow immediately upon return to his station.

Any important information obtained, together with suggestions regarding treatment, received either through reports sent to the Gas Service or based upon experimental information coming into possession of the Gas Service, will be forwarded immediately to the chief surgeon in order that it may be submitted to the chief consultant, director of general medicine, and medical officers of the American Expeditionary Forces.

The same information will be simultaneously supplied to our Allies through proper channels.

MEDICAL ORGANIZATION

In order to combat the results of this specialized warfare, a strong and coordinated medical organization is required to combine all natural divisions of relief, including organizations in the zone of the advance, organizations along the lines of communication, organizations at the base, and organizations for general research and development.

To perform properly the duties assigned to the Medical Department, the following measures looking toward the better prevention and treatment of gas casualties are hereby ordered:

(a) The institution of all practicable protective measures to prevent the depletion in strength of the fighting forces from avoidable causes in connection with gas warfare.

(b) The establishment of courses of instruction for intensive training of medical officers, nurses, and enlisted men of the Medical Department in the best methods of treating the gassed.

(c) The establishment of special centers for the treatment of gassed cases. The designation of the centers or hospitals will be made in orders from time to time.

(d) The appointment of specially trained medical gas officers with divisions; these officers to be known as division medical gas officers.

(e) The establishment at advanced aid stations of an efficient system and proper equipment for the administration of first aid for the gassed.

(f) The prompt evacuation of all gas casualties

(g) The supervision of the treatment of gassed cases entering all hospitals.

(h) The instruction of the rank and file in the theory and practice of first aid to gassed men.

H. L. GILCHRIST,
Colonel, Medical Corps.

INSPECTION REPORTS OF MEDICAL DIRECTOR, CHEMICAL WARFARE SERVICE ^c

HEADQUARTERS, GAS SERVICE, OFFICE MEDICAL DIRECTOR,

June 18, 1918.

From: Medical director of the Gas Service.

To: The chief surgeon, American Expeditionary Forces.

Subject: Extract from memorandum, chief of staff, 2d Division.

The following pertaining to the Medical Department, 2d Division, was extracted from memorandum, chief of staff, 2d Division, concerning the recent gas attack during which nearly 800 casualties occurred:

The evacuation of wounded, hospital service, and general efficiency of the Medical Department has been beyond criticism and has been just as well as it could have been done, in my opinion, in a complicated map problem.

All gassed men were promptly bathed at the dressing stations, their clothing taken away, and they were sent wrapped in blankets to the field hospitals.

H. L. GILCHRIST,
Colonel, M. C., National Army.

^c With a view to betterment in gas defense methods an important duty of the medical director, Chemical Warfare Service, especially early in our front-line work, was investigation of gas attacks on our troops, with subsequent reports and recommendations. The two reports which appear here are typical save that several of the early reports of the medical director show gas defense methods in certain organizations to have been far inferior to those described here.—Ed.

AMERICAN EXPEDITIONARY FORCES,
HEADQUARTERS, SERVICES OF SUPPLY,
OFFICE CHIEF OF GAS SERVICE, A. E. F.,

June 20, 1918.

From: Medical director, Gas Service.

To: Chief of Gas Service, American Expeditionary Forces.

Subject: Report of recent gas attack on 2d Division.

1. I am submitting report of the recent gas attack on the 2d Division, during which over 800 casualties occurred, principally among the members of the 6th Marines, 5th Marines, and the 23d Infantry.

2. The troops subjected to the gas attack were holding a very important sector along the American front, extending from Bois to Belleau, and were ranged from left to right in the following order:

2d Battalion, 6th Marines.

2 companies of the 6th Marines, M. G. Battalion.

1st Battalion, 6th Marines.

3d Battalion, 23d Infantry.

2 companies, 5th Marines, M. G. Battalion.

1 company of the 1st Battalion, 2d Engineers.

The first three mentioned organizations were in the thickest of the gas attack and, as a result, furnished the greatest number of casualties.

3. The area bombarded was about $2\frac{1}{2}$ km. long by 1 km. wide, in a sloping ravine, heavily wooded with a thick underbrush. The gas attack began about 2 a. m. on the morning of the 15th and lasted until nearly daybreak. During this time, mustard gas alone was used. The shells were thrown over at a very rapid rate, it being estimated that from 2,000 to 5,000 were exploded during the attack. In this connection, attention is invited to extract copied from the divisional diary relative to this attack:

June 14. During the night and continuing throughout the day, the entire front line and many points in the back area of the division sector were intermittently shelled with gas, intermixed with some high-explosive shells. The gas shelling was with mustard gas. Up to 11 p. m. reports received indicated the evacuation of 700 gas casualties and the evacuation not completed. 11.30 p. m. gas bombardment along the entire front and back areas still continues. On account of the gas in the Bois-de-Belleau, the eastern edge of these woods was held by a thin line, the remainder of the battalion being withdrawn to the vicinity of Hill 181, which was free of gas.

June 15, 1918. The shelling of our front line and numerous points of our back area with gas and high-explosive shells continued, but with decreased intensity. The casualties due to this shelling up to 6 a. m. June 15 were 771.

4. *Gas discipline.*—The general gas discipline and morale of the troops during the bombardment was good. From all accounts, proper gas alarms were sounded in ample time for the adjustment of respirators, but in view of existing conditions—a pitch dark night, exploding shells on all sides, heavy underbrush, expected attack from the enemy, and the fact that the troops were worn out from several days of incessant fighting during which time they had little or no rest—they were in a state of physical depression and in fit condition for the action of poisonous gases. Again, many were scattered throughout the area asleep on the ground, and during the rush and darkness a few of these men were not awakened in time to apply their respirators. Some of the men had their respirators knocked off by the explosion of shells, colliding with trees, underbrush, etc. Many were compelled to remove them in order to see, still others removed the facepiece alone, and retained the mouthpieces and nose clip. From a careful study of all conditions connected with this gas attack, it is the opinion that little, if any, criticism can be offered concerning the actions of the officers and men during the attack.

5. Of the total number evacuated, perhaps 200 were slightly, if at all, gassed, but considering everything—their run-down condition and the fact that they had been subjected to the fumes of poisonous gas at periods when their masks were removed—it is the opinion that the action taken in removing these men to the hospitals was wise and resulted in saving many of them.

6. Up to the present but 4 deaths have occurred from this attack, but from the appearance of some of the cases seen by me, there will probably be 10 or 12 others. The principal reason for this low mortality was due to the excellent method of evacuation, the early removal of

clothing and administration of baths, and the close proximity of the hospital to the gassed area. (See report of the chief of staff, 2d Division, marked "Inclosure A.")

7. The casualties resulting from this attack were immediately taken to the dressing station, where they were disrobed, bathed, wrapped in blankets, and later removed to the gas evacuation hospital at Luzaney, some 12 to 14 km. from the gassed area. At this hospital 775 gassed cases were received on June 14.

8. From the hospital at Luzaney, the cases were evacuated to Evacuation Hospital No. 7, at Montanglaust; Evacuation Hospital No. 8, at Juilly, and several hospitals in the vicinity of Paris. I was present at the gas hospital at Luzaney on Sunday afternoon, at which time a large evacuation was taking place. The chief surgeon of the division was present and had taken personal charge of the evacuation, which was handled in a very excellent manner. I visited the Evacuation Hospital No. 7, at Montanglaust, and examined 250 cases. The cases seen here presented symptoms of a slight nature, and it is the opinion that the large majority of them will be ready for duty within a week or 10 days. At the evacuation Hospital No. 8, at Juilly, I saw 152 cases. These cases presented symptoms of a much more severe nature than those seen at the former. (See analysis chart following.)

9. Attention is invited to the following table, which is the analysis of the symptoms of the cases seen under treatment at the above-mentioned hospitals:

Evacuation Hospital No. 7

Total number of cases examined, 250.

Those presenting symptoms of—			Burns of the—		
	Number	Percent		Number	Percent
Respiratory tract.....	197	80	Belly.....	0	0
Eyes.....	148	60	Back.....	11	4
Nose bleed.....	6	2.4	Axilla.....	2	0.8
Vomited.....	93	38	Scrotum.....	55	22
Burns of the—			Arms.....	6	2.4
Face.....	16	6.4	Hands.....	2	0.8
Neck.....	7	3	Thighs.....	9	3.6
Chest.....	5	2	Feet.....	1	
			Buttocks.....	1	

Evacuation Hospital No. 8

Total number of cases examined, 152.

Those presenting symptoms of—			Burns of the—		
	Number	Percent		Number	Percent
Respiratory tract.....	126	83	Back.....	25	17
Eyes.....	143	94	Axilla.....	11	7.3
Nose bleed.....	8	5	Scrotum.....	84	56
Vomited.....	63	41	Arms.....	13	8.6
Burns of the—			Hands.....	0	0
Face.....	72	47	Thighs.....	13	8.6
Neck.....	35	23	Feet.....	0	0
Chest.....	13	8	Buttocks.....	9	6
Belly.....	8	5.3	Legs.....	8	5.3

From this table it will be noticed that 77 per cent of the cases had eye infections, 81 per cent respiratory symptoms, 40 per cent burns of the scrotum, and 40 per cent had vomited.

10. *The symptoms.*—The symptoms presented by the casualties were typical of those produced by mustard gas. They were characterized at the beginning in a majority of cases by lachrymation and smarting of the eyes. The eruption in some cases occurred quite early, but in the large percentage was delayed for 48 hours or later.

11. The group of cases seen presented a large number of body burns, which can be accounted for as follows: Although the night was dry, the men were perspiring badly, and due to the conditions existing at the time of the gas attack they were obliged to crawl around among the thick underbrush, which was thoroughly saturated with the gas. In many cases their clothing was torn from their bodies, their hands and faces scratched, masks brushed from their faces, etc. Nearly all were obliged to lie down at some time during the attack.

12. *Respiratory tract.*—Of the cases seen, 81 per cent had symptoms of irritation of the respiratory tract. Laryngitis and bronchitis were present in a large percentage of the cases, especially in Evacuation Hospital No. 8, where a few cases were developing bronchial pneumonia. I think the face burns examined were of a much more severe nature than any yet seen, and in all cases the men acknowledged that their respirators were either removed or knocked off sometime during the bombardment.

13. *Lesions of the eyes.*—At Evacuation Hospital No. 8 a large number of the cases presented inflammation and puffing of the eyes, with the usual conjunctival irritation.

14. *Summary.*—(1) The large percentage of casualties resulting from this attack was not due to lack of proper discipline and gas morale.

(2) That the low mortality was due to the excellent method of evacuation and to treatment that cases received when arriving at the hospitals.

(3) That the results of this gas attack show most emphatically the necessity of the early removal of clothing and bathing of all men subjected to mustard gas attacks; also the importance of having gas hospitals as close to the front as possible, where advance treatment can be given.

15. During this investigation every assistance was offered me by the officers of this division. Major General Bundy, in command of the division, was highly pleased at a visit from a representative of the Gas Service to conduct this investigation.

H. L. GILCHRIST, *Colonel, Medical Corps.*

HEADQUARTERS SECOND DIVISION (REGULAR),
AMERICAN EXPEDITIONARY FORCES,

France, June 16, 1918.

Memorandum for Colonel Gilchrist, Medical Corps:

The gas discipline of the men is excellent, and every man had and used his mask. The casualties were largely due to body burns, caused by clothing saturated with mustard gas. These we consider unavoidable casualties, when it is recognized that the troops occupied wooded and thickly grassed positions which had to be held.

The evacuation of wounded, hospital service, and general efficiency of the Medical Department has been beyond criticism and has been just as well as it could have been done, in my opinion, in a complicated map problem.

All gassed men were promptly bathed at the dressing stations, their clothing taken away and they were sent wrapped in blankets to the field hospitals.

The approximate number of gas casualties is 900, but it must be borne in mind that the division is under a constant and violent bombardment of gas and high explosive of all calibers, with gas mixed in with shell and shrapnel.

PRESTON BROWN,
Colonel, General Staff, Chief of Staff.

HEADQUARTERS 2D DIVISION,
AMERICAN EXPEDITIONARY FORCES,
France, June 16, 1918.

From: Chief gas officer, 2d Division.

To: Commanding general, 2d Division.

Subject: Gas attack.

1. A severe bombardment of high-explosive shrapnel and gas shell occurred on the morning of June 14.

2. The area bombarded was about 2 km. long by 1 wide, in a wooded ravine extending east of Lucy-le-Bocage along the southeastern edge of Bois de Belleau.

3. This bombardment began about 2 a. m., while a relief was taking place. For two hours the shelling was very intense, one officer estimating a rate of 10 shells per minute per 100 square yards; another, "as fast as it was possible to put them over." It continued less intensely during the entire day. Mustard gas used extensively.

4. The troops subjected to this were the 5th and 6th Marines and part of the 23d Infantry, with some men of the 2d Engineers, 6th Machine Gun Battalion, 1st Field Signal Battalion, and Medical Department. About 2,500 men were in the area. These troops were either men who had been holding this line for 15 days or freshly arrived replacements, under fire for the first time.

5. The morale was on the whole good, the gas alarm being given and respirators being adjusted, but in their anxiety to get out of the terrific fire many removed their respirators, or merely the facepiece, so as to be able to see more clearly and thus get out of the shelling more quickly.

6. The majority of the casualties occurred among these troops, who, although not remaining in the area for a great length of time, had been under such a strain for the past two weeks and were physically in such a weakened condition that a slight amount of gassing, which ordinarily would not have affected them, proved too much for their run-down systems.

7. Fully 200 out of the total of 850 were evacuated who really were not gassed, but showed slight signs of being affected, and it was deemed best to send them back rather than have them become serious casualties later on.

8. Two companies in the edge of the woods, where the gas was not so thick, remained in their position until 5 p. m., when they received authority to evacuate it. The troops here wore their respirators for three or four hours and intermittently the balance of the day, but gradually felt the effects of the dilute concentration, and many were slightly gassed.

9. Apparently comparatively few showed signs of lung irritation, the majority being affected in the eyes or burned on the body. These burns are accounted for by the men being compelled to crouch down in the gas-affected ground or push their way through bushes and undergrowth which had been splattered with gas.

10. In summing up, I should say that under the conditions the casualties are not excessive. Under the same conditions, moreover, had the men been fresh instead of worn out, the number of slight casualties would have been greatly reduced.

RUGER W. HAY, *Captain, Engineers, U. S. R.*

AMERICAN EXPEDITIONARY FORCES,
HEADQUARTERS SERVICES OF SUPPLY,
OFFICE MEDICAL DIRECTOR, GAS SERVICE,
July 2, 1918.

From: Medical director, Gas Service.

To: Office chief surgeon, Services of Supply, American Expeditionary Forces.

Subject: Report of gas attack.

1. Herewith inclosed report of investigation of gas attack on the 2d Division June 23, 1918.

H. L. GILCHRIST,
Colonel, Medical Corps, N. A.

AMERICAN EXPEDITIONARY FORCES,
HEADQUARTERS, SERVICES OF SUPPLY,
OFFICE CHIEF OF GAS SERVICE,
July 1, 1918.

From: Medical director, Gas Service.

To: Chief of Gas Service, American Expeditionary Forces.

Subject: Report of second serious gas attack in 2d Division.

1. I wish to make the following report relative to the gas attack which took place Sunday evening, June 23, in the 2d Division, from which resulted 414 casualties. This is the second gas attack which has taken place in the division during the present month, the former one occurring on the nights of June 14 and 15, resulting in over 800 casualties.

2. The recent gas bombardment took place in the sector of the line midway between Bouresches and Vaux, and covered an area $1\frac{1}{2}$ km. front by 2 km. deep. The part bombarded was in a heavily wooded valley, with much underbrush, and was occupied by troops from the 9th and 23d Infantry.

3. The bombardment began at 10 p. m. and lasted an hour, during which time shells were discharged at the rate of about 15 per minute. The night was warm and dry, with a slight breeze blowing from the north, which later changed to the northwest. Following the bombardment there was a lull of nearly three hours during which time occasional shrapnel and artillery shells were exploded. At about 1 a. m. the gas bombardment was renewed with increased vigor. This attack lasted about 50 minutes, during which time gas shells were discharged at a greater rate than during the earlier attack. "Mustard" seems to have been the principal gas used, with a possibility of a slight mixture with other gasses.

4. The following extract was taken from the war diary at division headquarters relative to this attack:

June 24, 6 a. m. Attack of the 3d Battalion, 5th Marines, against the northern part of Bois-de-Belleau on the evening of June 23 proved successful. During the night the 3d Brigade, 9th Infantry, and 23d Infantry was subjected to a heavy gas bombardment intermixed with high-explosive shells for a period of seven hours. The Boise-des-Clerambouts was evacuated and is held only by a few patrols.

Gas casualties reported:

9th Infantry.....	152
23d Infantry.....	162
5th Machine Gun Battalion.....	25

Casualties not all reported.

5. The casualties resulting from the bombardment were removed to the dressing station at Bezu-le-Guery, about 5 km. behind the line and from there evacuated to the special division gas hospital at Luzaney, some 8 km. farther back.

6. Up to the time of my visit, which was three days following the bombardment, no deaths had been reported as result of this attack, but from the serious condition of many of the casualties examined by me it is the opinion that several will succumb.

7. Due to the excellent system of evacuation of wounded from this division, a large number of the casualties had been transferred to distant hospitals before my arrival; as a result I was permitted to examine a limited number. The following table is an analysis of the symptoms of those examined:

Total number of cases examined, 46.

	Number	Percent		Number	Percent
Those representing symptoms of—			Burns of the—		
Respiratory tract.....	41	90	Chest.....		
Eyes.....	41	90	Arms.....	1	2
Vomited.....	26	57	Axilla.....		
Nose bleed.....	4	8	Serotum.....	17	37
Burns of the—			Thighs.....	4	8
Face.....	5	10	Buttocks.....	1	2
Neck.....	2	4	Hands.....		
Back.....			Feet.....		

8. The symptoms presented by the casualties were typical of those produced by mustard gas and nothing unusual was noted. It might be well to state, however, that the respiratory conditions appeared to be more severe than those seen on former groups.

9. The principal causes of the casualties (340 cases needing medical care) during this attack were as follows:

(1) Delay in applying respirators, and their promiscuous removal during and premature removal following the bombardment.

(2) Relying on poorly constructed dugouts.

(3) Failure to awaken sleeping men.

(4) Permitting men to enter an old mill in the gassed area and to remove their masks.

10. After careful analysis of the conditions associated with this attack it is the opinion that many of the casualties were the result of individual carelessness and, to a certain extent, poor company gas discipline. Of course, the fact must not be lost sight of that the members of these organizations were heavily engaged with the enemy for the past two or three weeks, during which time they have been subjected to many hardships, which has resulted in a general lowering of their physical condition, thereby rendering them in a fit state for the actions of poisonous gases. Nevertheless, considering everything in connection with this bombardment—the lowered physical condition of the men, the nature of the attack, darkness, heavy underbrush, poorly constructed dugouts, and permitting men to enter a gas-saturated building, etc.—it is the opinion that with proper care many of these casualties could have been averted.

11. From interviews with casualties resulting from this attack few seemed to be familiar with the question of mask removal during and following gas attacks. Some were of the opinion that they removed their masks immediately after the bombardment ceased; others stated they did not remove them until they saw their officers without masks, and still others said they removed them at intervals during the bombardment for the purpose of obtaining better vision or because the respirators were uncomfortable. Few had received orders of any kind from officers or others relative to removal of masks.

12. The dugouts appear to have been one of the principal causes for the gas casualties. These dugouts, from all accounts, were but mere holes of different sizes dug in the side of the trenches, some capable of holding two men, others more; all were protected by hanging curtains made of shelter halves dropped in front. The men entered these places thinking they were safe and removed their masks; as a result many became gassed.

13. Many men were gassed in an old mill which was in the midst of the gassed area. Following the bombardment the men entered this place, removed their masks, and laid down on the gas-saturated hay-covered floor to rest. All stated the odor of gas was very strong at the time, but inasmuch as their officers were present without masks they thought the place safe. Many men were gassed because they were not awakened when the gas attack began. Others stated they smelt the gas long before any gas alarm was sounded.

METHOD OF EVACUATING GAS CASES AND THEIR TREATMENT

14. The method of evacuation of gassed casualties and their treatment at the dressing station has been carried out so successfully in this division that a brief description of the methods will be given. When gas casualties occur they are immediately removed to the dressing station, which at present is established at Bezu-le-Guery and is operated by Field Hospital No. 1, United States Army. It occupies the church adjoining schoolhouse and two or three near-by buildings. It is divided into sections—the operating section, dressing section, degassing section, and administrative section. Two tents have been erected adjoining a small building fitted up as a bathhouse, which are used for gassed casualties. Here they are stripped and assigned to the baths, those presenting serious symptoms are not permitted to get up but are bathed on litters in a reclining position; the others are marched into the bathhouse, where they are given hot baths. The bathhouse is equipped with a portable heating apparatus connected with six shower heads. After the men have been bathed and dried, their eyes, noses, and throats are sprayed with a solution of bicarbonate of soda, following which they are re-dressed in pajamas and removed to the church, which is fitted up as a temporary hospital. From here they are evacuated to the special gas hospital at Luzancy as soon as possible. The administrative and operating part of the dressing station is located in the schoolhouse.

15. At the commencement of a gas bombardment the commanding officer of the dressing station is notified by messenger, thereby giving him ample time to prepare for the reception of the casualties. A special medical officer, with enlisted assistants, has charge of the degassing tent and baths; another is responsible for the irrigations; and others are responsible for administration of proper nourishment, etc. The men in the degassing section wear rubber gloves and aprons when handling the patients and when handling the seriously gassed wear the French M. 2 masks. The success of the organization depends upon simplicity of methods, strict discipline, and thorough organization.

16. Attention is again invited to the subject of long hair in connection with gassed cases. This matter has been taken up before and recommendation made that all men in the front area be compelled to have the hair on their heads closely cropped. I am firmly convinced that long hair on the head has much to do with the harboring of poisonous gasses, thereby being responsible for many men being gassed after the removal of their masks. All medical officers interrogated relative to this subject are of the same opinion. It is again recommended that all men serving in the front areas be compelled to have their heads closely cropped.

17. *Gassed casualties in this division.*—It might be well to invite attention to the number of gassed casualties that have occurred in this division since the 1st of June, which will serve the purpose of giving some sort of an idea of what may be expected from other divisions after they enter the front area. From figures obtained from the division commander it appears that from June 1 to 6 a. m. on the morning of June 27 there had been 1,924 casualties in this division from the effects of poisonous gasses. At present it is impossible to state the number of deaths, but from the available figures obtained from the office of the chief surgeon, American Expeditionary Forces, and other sources it appears that the mortality list will be between 2 and 2½ per cent. The commanding general of this division is greatly interested in gas matters and it appears has made every attempt to enforce rigid obedience of gas orders; notwithstanding there have been cases of apparent lack of gas discipline on the part of individual company commanders which have resulted in gassed casualties.

H. L. GILCHRIST,
Colonel, Medical Corps, N. A.

REPORTS OF DIVISION SURGEONS, 42d Division.^d

FIRST REPORT

GAS PROTECTION AND INSTRUCTION

The use of gas in modern warfare had become extensive and, unless great precautions were taken, produced so many casualties that it became one of the big problems with which we had to deal. Shortly after arrival at the front it became evident that there were certain essential features connected with gas warfare that could not possibly be handled by line officers acting as the divisional gas officers. It was seen that a medical officer specially elected and trained was an absolute necessity in order to properly cover the medical aspects of the case. This idea was followed; an officer was selected, sent to the British front for instruction, and then attached to the division surgeon's office, but without any official definite status. His work, however, proved of such value that he was designated division medical gas officer by a division order (Memorandum 148, II. Q., 42d Division, April 23, 1918). This was the beginning of the division medical gas officers of the American Expeditionary Forces, inasmuch as the idea was adopted by higher authorities and the office authorized for each division in the American Expeditionary Forces by a general order from General Headquarters. His duties consisted in instructing medical personnel, commissioned and enlisted, in gas defense, supervision of gas protection of medical dugouts, aid and dressing stations and field hospitals, and particularly to instruct medical personnel, commissioned and enlisted, in the early symptoms, diagnosis, and treatment of gas casualties of all types. In modern warfare this work is extremely important, and if properly followed will result in the saving of many lives, of the shortening of the period of disability in a large number of cases, as well as altogether preventing the occurrence of gas casualties in many instances.

Memorandum No. 118.

HEADQUARTERS 42D DIVISION,
OFFICE OF THE SURGEON, A. E. F.,
April 24, 1918.

DEFENSE MEASURES AGAINST GAS, MEDICAL DEPARTMENT

To surgeons of all organizations:

1. Every officer is responsible that the men under his command are carefully instructed in defense measures against gas that they will properly protect themselves and intelligently aid those who have become casualties from exposure to gas.

Familiarity through continuous training with the means supplied to combat gas attacks and with the procedures necessary for the successful relief of those affected by poisonous gas is required of all officers and men.

2. Standing orders on defense against gas, April 18, 1918, must be strictly adhered to, and special orders here detailed must be rigorously enforced.

A. Standing orders which should be given special attention are:

I. Carriage of respirators and masks in prescribed zones.

II. Training in quick adjustment of respirators.

III. Practice in the use of antigas appliances.

IV. Alarms and warnings.

B. Special orders on defense against gas:

I. Besides the usual inspection of respirators and masks, there shall be an additional inspection before sanitary troops proceed into forward areas.

II. Proficiency must be acquired in the quick adjustment of respirators and masks, especially as concerns holding the breath both at inspiration and expiration. A deep breath may fill the lungs with air contaminated with gas with disastrous results.

III. Practice in adjustment of respirators and masks to those impersonating helpless men is required twice weekly.

^d The first of these reports was made by Lieut. Col. J. W. Grissinger, M. C., division surgeon; the second and third by Col. D. S. Fairchild, Jr., M. C., who succeeded the former officer as division surgeon.—Ed.

IV. In the event of a cloud gas attack or gas-shell bombardment—

- (a) Gas-proof dugouts will be closed immediately.
- (b) Fires in dugouts will be extinguished and chimneys closed.
- (c) A sentry will be posted inside the entrance curtain to prevent the entrance of men whose clothing is known to be contaminated with gas, until such clothing is removed.
- (d) Litter bearers will completely close the outer curtain, before opening the inner one, when entering medical dugout.

Drill with loaded litters, observing these precautions, is required.

V. Medical dugouts should be sprayed frequently and the blanket protection kept moist with a solution containing—

Hexamine.....	grams..	70
Sodium sulphite.....	do.....	115
Sodium thiosulphite (hypo).....	do.....	195
Water.....	liters..	4

Heat slightly to dissolve.

This solution will neutralize small amounts of gas admitted during frequent entrance to dugouts. Tissot respirators should be worn, if necessary.

For ordinary moistening of blankets the following solution should be used:

Sodium carbonate (washing soda).....	grams..	240
Sodium thiosulphate (hypo).....	do.....	480
Water.....	liters..	4

Owing to the corrosive action of these mixtures they must not be kept in vermoral sprayers, as the apparatus will be ruined.

VI. Care must be taken that men sleeping in closed spaces are not gassed by long exposure to small quantities of gas unknowingly brought in on their clothing or equipment.

VII. No man affected by gas, however slightly, will be allowed to walk to a dressing station or to exert himself physically in any way.

VIII. Precautions will be taken to protect surgical instruments and appliances from the corrosive action of gas.

IX. Lyster bags must be carefully and completely covered to prevent contamination from gas.

X. It is forbidden to use water from shell holes for drinking, cooking, washing, or bathing.

XI. Food which has been exposed to gas must be destroyed.

XII. To provide for clearing of dugouts by fire, a waterproof receptacle must be kept in each dugout containing dry wood, chips, and paper, together with a 4-ounce bottle of kerosene. (A bacon can supplied with a good cover will answer the purpose.)

3. Mustard gas: I. Anyone close to the burst of the gas shell may have some of the liquid sprayed on his clothes. When possible, the clothes will be removed.

II. If mustard gas is present, the area is dangerous usually for one or two days, and sometimes for four days, or even longer. The area is to be regarded as dangerous as long as the odor of mustard gas can be detected. The danger of mustard gas lies in its insidious nature, because no appreciable irritation either of the eyes, throat, or skin is produced at the time.

III. If there is a suspicion that mustard gas has touched the skin, it should be powdered with chloride of lime and then washed thoroughly with soap and water. If these are not available, thorough washing with pure water will aid materially.

IV. Do not put the fingers in the eyes or mouth, scratch the skin, or touch the genitals or anus, and thus risk contamination with mustard gas, unless the hands have been disinfected.

V. Mustard gas is promptly diffused in the presence of heat. Therefore no man wearing or bearing contaminated clothing will enter any heated room or dugout.

VI. The use of latrines in an infected zone should be immediately forbidden until they have been disinfected and washed with chloride of lime.

VII. With a view of obtaining, in the methodical disinfection of ground bombarded by mustard-gas shells, the most complete results possible, it is necessary to give particular instruction to a certain number of men who will form detachments furnished with all necessary materials.

A disinfecting detachment comprising one none commissioned officer and six privates should be used, provided they are not required for the service of the wounded. In the latter event, disinfection will be accomplished at the earliest possible moment.

VIII. Those who handle gas cases and their discarded clothing and equipment must be properly protected by gas masks, antigas clothing, and oilcloth mittens and be provided with tongs or pincers.

4. Antigas stores;^e

Alarm devices.	Gas caps.	Sodium chloride.
Box respirators.	Gas coats.	Ammonia ampules.
Masks.	Oilcloth mittens.	Camphor in oil.
Extra eyepieces.	Soap.	Morphine.
Tissot respirators.	Needles.	Cocaine.
Gas-proof coverings for dug-outs.	Thread.	Medicine droppers.
Vermoral sprays.	Tongs or pincers.	Ambrine.
Solution jars.	Nails.	Oxygen tanks and connections.
Buckets.	Shovels.	Catheters for oxygen administration.
Antigas fans.	Chloride of lime.	Rubber tubing.
Fuel for clearing dugouts.	Hexamine.	Gauze.
Four-ounce bottles for kerosene.	Sodium thiosulphate (hypo).	
Oilcloth.	Sodium sulphite.	
	Sodium carbonate.	
	Sodium bicarbonate.	

BANDAGES

Commanding medical officers of units relieving one another are responsible that the stores are properly taken over.

The divisional medical gas officer will make arrangements for the weekly inspection of all antigas stores. Commanding officers should take this opportunity to inform the D. M. G. O. or his N. C. O. of any stores which are deficient or damaged.

5. Treatment of gas casualties:

A. Aid stations—

- (1) Retain masks on patients until danger is over.
- (2) Avoid unnecessary movements.
- (3) Ammonia inhalations by litter bearers to all cases with dyspnea.
- (4) Loosen or remove clothing; remove equipment.
- (5) Encourage vomiting by tepid salt water.
- (6) Avoid atropine.
- (7) Attention to eyes of mustard-gas cases.
- (8) Administer oxygen, if necessary.
- (9) Evacuate promptly as litter cases.

B. Dressing stations—

- (1) Keep patient recumbent in open air if possible.
- (2) Ammonia inhalations.
- (3) Oxygen, if possible.
- (4) Morphine for restlessness.
- (5) Treat eyes of mustard-gas cases (cocaine 2 per cent, if necessary).
- (6) Retain shock cases for treatment (warinth, camphor in oil).
- (7) Evacuate cyanosed cases quickly for oxygen treatment.

C. Gas hospitals—

- (1) Relieve of equipment in receiving room.
- (2) Remove clothing in disrobing room.
- (3) Bathe under hot-water showers, using an alkaline soap (lying and sitting cases).
- (4) Irrigate eyes and burns with alkaline solution, and supply with clean clothing or blankets.
- (5) Remove to wards on litters.
- (6) Separate mild from serious cases.
- (7) Treat shock (heat, camphor in oil, pituitrin).
- (8) Morphine for restlessness.
- (9) Ammonia inhalations during first 24 hours only.

^e For other supply lists see Appendix, pp. 831, 832.—Ed.

- (10) Posture for edema: Raise the foot of the bed.
- (11) Pure oxygen for chlorine and phosgene cases.
- (12) Venesection for congestive cases.
- (13) Liquid diet first day.
- (14) Mild purge third day.
- (15) Expectorants after second day.
- (16) For cough, mild sedatives and spray of albolene and eucalyptus.
- (17) Treat burns with ambrine when necessary; use no fatty ointments.
- (18) Wounded cases to have special attention.
- (19) Reserve masks to the number of 20 per cent of the maximum bed capacity to be always on hand.
- (20) A mask or respirator will be hung at the head of the bed of every patient, for emergency use.
- (21) Contaminated clothing will be sterilized and laundered before being reissued.

6. Solution for irrigating eyes of mustard-gas cases:

Sodium bicarbonate-----	grammes--	150
Sodium chloride-----	do-----	70
Water-----	litres--	5

Apply warm as an irrigation to eyes and nose, and use on compresses continuously in the acute stage.

7. It is directed that a copy of this memorandum be furnished each medical officer in your command.

J. W. GRISSINGER,
Lieutenant Colonel Medical Corps, U. S. A.,
Division Surgeon.

SECOND REPORT

FIELD HOSPITAL AS GAS HOSPITAL

Before entering this engagement (Aisne-Marne), guided by the large number of gas casualties reported by the divisions in the line, it was decided to set aside one field hospital, to function entirely as a gas hospital, whose duty it would be to produce a teamwork system that would insure both speed and efficient care in the treatment of the gassed. Field Hospital Company 167 was designated as the gas hospital, and ever after during active operations continued to specialize in this line. The scheme devised by this organization was crystallized into its final form during the operations at Bezu-St. Germaine and is described briefly below.

Upon assuming the functions of a divisional hospital for the treatment of gas casualties it became necessary for Field Hospital Company 167 to modify and add to its equipment and to specialize its personnel. Additions to the equipment were as follows: A portable bath equipment; additional oxygen tanks and connections; chemicals required for the various alkaline solutions; clothing surplus; oilcloth gloves and clothing for protection of personnel.

(1) For a receiving ward, a ward tent was always used so that when weather permitted the walls could be rolled up and adequate ventilation be thus obtained. Here the patient, always recumbent, was examined and his clothing was removed, during which time records were taken and field cards started by a force of clerks circulating among the patients. As quickly as possible all hair was clipped and the patient was wrapped in blankets. At this time a bag was supplied for personal effects, which always accompanied the patient, thus eliminating the checking system which at all times, and especially in rushes, was found to be most unsatisfactory. The patient was given a 2-ounce dose of an alkaline solution internally and was then carried to the next room.

(2) The bath and treatment room was usually in a ward tent, though when available a building was sometimes used. Here patients were placed on horses [wooden] under shower heads, the litters being protected by rubber blankets. Conveniently placed was a series of irrigating vessels with rubber hosing and nozzle attachments. By means of these, alkaline irrigation of the eyes, ears, nose, mouth, axillae, and genitals was accomplished while the rest of the body was being treated with alkaline soap. Then a full bath in comfortably warm water was given. This finished, other details were ready to dry, powder, and provide clean hospital clothing.

(3) The patient was then ready to be taken to his ward and put to bed. In so far as possible, the cases were placed and classified according to severity and also to kind of poisoning. Each ward was provided with oxygen, stimulants, heating appliances, and blood-letting outfits. Here the patient remained until it was deemed advisable to remove him to the (4) evacuation ward. This system was so devised that the current of patients and attendants was always in one direction. Every effort was made to obtain a rapidly moving and smoothly working system so that, when necessary, a large number of cases could be passed through as quickly as possible. The personnel was divided into various teams, each with a definite part of the work to perform. So adept did these teams become that when the occasion arose it was possible to pass patients through at the rate of one every three minutes.

THIRD REPORT

MEDICAL GAS DEFENSE

The duties of the Medical Gas Department before and during the service of the 42d Division in the Lorraine sectors consisted of instructing and training members of the division in the methods of defense against gas warfare.

Some knowledge of the various kinds of gases already in use, as well as the markings of projectiles and containers, was made known, and definite information regarding protection against new gases was supplied to all medical officers and gas N. C. O.'s who were established in the areas exposed to gas.

In the matter of protection, all troops were instructed thoroughly and frequently in drill with respirators and masks, which were inspected daily in the alert zone and weekly in the ready and precautionary zone. Five per cent extra gas-mask equipment was kept on hand, together with antigas stores.

All stretcher bearers and first-aid men carried ammonia ampules, and were instructed in their use; they were also warned of the necessity of the proper adjustment of respirators to casualties within the gassed area; and for even mild cases, were advised of the danger from exertion.

To render dugouts tenable, they were constructed so that all chimney openings could be sealed perfectly, and no passage was constructed which was not protected by double doors, these doors being 3 feet wide and placed at least 8 feet apart, to permit the entrance of an occupied litter, so that the outer blanket could be properly arranged before the inner one was opened. Blankets for these openings were made sufficiently long to cover the frame without touching the ground, and were 4 to 6 inches wider than the frame, so that when they were in place they would fall over the edges. By nailing a lath to the top of the frame, tearing was prevented; another lath, tacked at the bottom, made a core upon which the blanket was rolled when not in use at the top of the frame, the rolled blanket being held in position by a string tied in a slip knot to allow of instant dropping in emergency. Weights were sewed into the free edges of the blanket to secure perfect closing. These curtains were kept impervious to gas by saturation with water or other fluid. For this purpose a Vermoral sprayer was kept at hand to be used twice daily, or as often as necessary.

Within the dugouts at least two Ayrton flappers for cleaning the approaches were kept, together with a moisture-proof tin box, containing dry wood, paper, and a small bottle of kerosene for clearing the chambers by fire. Approximately 1 pound of fuel to 200 cubic feet of air space was required. A bright-burning fire, without smoke, 6 inches off the floor, in the center of the room, was found to be the best means for clearing it from gas which may have entered at some opening or have been carried in on the clothing of casualties or litter bearers. In addition, the interiors of the chambers were sprayed occasionally with a Vermoral sprayer containing a solution of—

Hexamine.....	ounces..	2½
Sodium sulphite.....	do.....	3¾
Sodium hyposulphite.....	do.....	6½
Water.....	gallon..	1

The solution was heated in the making and thereafter kept in stoppered jugs, or other nonmetallic containers. On account of its corrosive action, it was not kept in Vermoral sprayers.

The treatment of gas casualties at the front consisted in administering ammonia to those with dyspnea, relieving the constriction of clothing and equipment, removing clothing contaminated with gas before entering the dugout, and using precautions against chilling.

Oxygen was supplied through fresh air or artificially. There was kept on hand a number of small tanks of oxygen, with tubing attached, containing sufficient gas to last during a part at least of the time of transportation to evacuation hospitals.

For the burning effects of mustard gas, bleaching powder, in the proportion of 4 ounces to the gallon of water, was used, recent experiments having proved its efficacy. Treatment generally aimed to accomplish the following: (1) To diminish the respiratory activity of all gassed cases as far as possible; (2) to improve the supply of oxygen; (3) to combat the pulmonary edema and inflammatory changes in the lungs; (4) to keep up the circulation; (5) to promote the excretions of poison from the body; (6) to prevent the onset of secondary infections; (7) to alleviate the pain and discomfort; (8) to keep the patient warm.

With the removal of casualties to hospitals, treatment was instituted immediately, bearing in mind that as little exertion as possible should be made by those gassed. Those of congestive type were relieved by venesection, 1 or 2 pints of blood being removed, care being taken subsequently to restrict the fluid intake. Administration of oxygen over a considerable period of time, 4 minutes out of every 15, was of paramount importance. The Trendelenburg position relieved some of the embarrassment of respiration by draining the bronchii and thereby also relieving the cough. Artificial respiration and stimulation with ammonia, camphor in oil, and strychnine were given in emergency. Morphine was useful as a sedative, and mild expectorants for the cough. Atropine and digitalis were contraindicated.

Various schemes for the administration of the oxygen were devised, mostly with the idea of supplying a large number of cases from a few tanks of gas. The multiple tube attachments seemed most desirable, those of the overhead piping giving the cases at the end of the line a dearth of gas.

The treatment of mustard-gas casualties required a totally different procedure, and the one followed by the French was adopted. A building set apart was subdivided, and an entrance room for the reception of cases contained benches and a number of slotted tables, where all clothing was removed from those gassed, both simple cases and those cases complicated by wounds, a numbered bag being issued to each man for his personal belongings. A communicating shed contained tanks, 10 by 10 by 10 feet, filled with water or a solution of bicarbonate of soda, in which clothes were allowed to soak from 3 to 12 hours before being hung in the open. This solution was not allowed to boil, for steam vaporized the mustard gas. From the receiving room the men were taken to the shower room, which was heated and where a thorough bath with hot water and soap was given, particular attention being paid to hairy parts. The wounded were bathed on slotted tables placed under the showers and, after bathed, were given fresh clothing or blankets and removed to the wards for warmth and local treatment. The eyes were flushed frequently with a solution of—

Carbonate of soda.....	grams..	150
Sodium chloride.....	do....	70
Water.....	liters..	5

Cocaine and ice compresses were used for the relief of pain.

These cases suffered considerably from involvement of the areas most plentifully supplied with sweat glands, most notably the genital and axillary regions, and a soothing ointment with a fatty base, lanoline with chloramine-T for the mild and ambrine for the severe type of dermatitis was used with good results.

Men detailed to handle and to treat the contaminated material wore special gloves which had been saturated with boiled linseed oil; soft soap rubbed into canvas gloves gave protection for a short time.

The gas casualties while on the Lorraine front were 517 between February 23 and March 25, 1918. The report of the number of gas casualties on the night of March 20 and 21 showed 5 officers and 197 men, the gas used principally mustard, although there were clinical reasons to prove that other gases also were sent over either individually or in combination with mustard gas. The containers were gas shells.

There were definite reasons for this large casualty list, some legitimate, but, for the most part, preventable; first, there was shown to be insufficient training in gas defense, and, second, disciplining was insufficient. The element of ignorance of the definite rules for gas defense as expressed in the various ways was shown by the character of the casualties and the excuses given. The majority of the cases showed burns over the entire face and lung involvement of a serious nature, proving conclusively that respirators were adjusted too late, not worn

at all, or removed too soon. An analysis of the excuses for gassing showed that the serious consequences possible were not considered by many in the event of small amounts of gas which were put over at the same time as high explosives, and explained some legitimate casualties, and besides the atmospheric conditions were ideal for the use of gas.

The gas casualties at Baccarat, on the Lorraine front, were 430 between April 23 and June 19, 1918. An effort was made in each individual case to verify the symptomatology, and to ascertain if possible the exact conditions, circumstances, and time when patients received the gas. As an example, the 150th Field Artillery were shelled by gas on May 2 and 3, resulting in 16 casualties. Observations were made as follows: One man received gas by running into an unprotected dugout, opening into a shell pit, after the air in the open was apparently clear. Another was badly burned in repairing telephone wires which had been put out by a gas shell. Still another was gassed while running by a field piece which had received a direct hit. One was gassed in a gun pit, while working on the gun, by a shell which struck the side of the pit and sprayed the piece. The next man, from symptomatology, was probably gassed the day before by a shell that struck less than 10 feet away. Another was gassed by coughing off his gas mask, while bringing up shells. One case was asleep in the kitchen when it received two direct hits, the first spraying the front door with gas, the second landing directly on top. Two were probable malingerers.

The symptoms were as follows: Three cases had burns which were their most prominent symptom; a number of others complained of respiratory embarrassment, first noticed when walking away from the guns after relief, but attributed at the time to fatigue; still others complained of sore throat and said, "They felt as though their throats were extremely dry and parched," and one man was burned from knee to ankle by a contaminated puttee.

Aside from the medical interest, it was rather remarkable that these men were able to operate their guns continuously throughout the period of action, although practically deluged with gas five times within 36 hours, the last shelling being mixed with high explosives in the ratio of about 1 to 4.

The next engagement was on the Champagne front, from July 12 to July 19, 1918; while of short duration the bombardment from the enemy was most intense. The damage, however, from a gas standpoint was of little importance, our casualties being only 116 in number, mostly slight cases. The proportion of high-explosive to gas shells used here was greater than usual, and the type of gas used less dangerous.

The Chateau Thierry front, where the type of warfare changed from defensive to offensive, necessitated also a change in the divisional methods of handling gas casualties. In the Luneville and Baccarat areas, patients had been evacuated to the evacuation hospitals, which were in neither case over 12 miles from the line. Here, however, and on later fronts, these hospitals were so far in the rear that it became necessary to use one of the four divisional field hospitals for the care and treatment of gas casualties, and it became known as the division gas hospital.

In the St. Mihiel sector, from September 12 to 21, 1918, the casualties were slight, only 78 gassed cases being received in the divisional gas hospital, of which 31 were returned to duty in from one to three days.

From October 8 to the time of the signing of the armistice, the division was on the Argonne front, and casualties from gas were high, due in part to the wooded nature of the country. Of the 1,129 cases received at the advanced dressing station, 481 were returned to duty from the division gas hospital after from one to five days of treatment and observation.

From experience, it is the belief that a gas hospital may be successfully operated either as a stationary or as a movable unit, with the present personnel of a field hospital as indicated in the Tables of Organization, if augmented by a sufficient number of teams thoroughly trained in the treatment of acute poison-gas casualties and certain necessary additions to equipment.

A field hospital under canvas commanded by a major, assisted by 5 junior officers and an enlisted force of 83 men, is capable under ordinary circumstances of caring for as many gas casualties as may be transported by the 48 ambulances of a division, if the capacity of the hospital is limited to its maximum of 400 patients. If, however, such a unit be in tents, barracks, or permanent buildings should be called on to care for more than its tent capacity of 400 patients, sufficient help could be obtained by the temporary assignment of previously trained teams of three medical officers and 5 nurses for each 200 patients.

SECTION II

CLINICAL FEATURES

CHAPTER V

PHYSIOLOGICAL ACTION OF WAR GASES

TOXICITY

The first outstanding feature of the war gases is their very high toxicity. They kill where substances measuring up to our former ideas of high toxicity fail to injure. Thus prussic or hydrocyanic acid, which has usually stood at the head of toxic gases in the minds of scientists and laymen alike, is no more toxic, as a matter of fact, than a dozen other gases which were investigated or tried out in the war. In the field it proved practically harmless. The toxicity figure for chlorine is about 2.5 mg. per liter; that of phosgene 0.35; for mustard gas, hydrocyanic acid, and a considerable number of others, 0.2 or less.

The peculiar requirements for field use, as contrasted with controlled laboratory administration, was responsible, of course, for the fact that hydrocyanic acid was found almost useless as a war gas, while the commonly handled chlorine, produced industrially in such large amounts every day without accident, proved so very potent in war and the insidious phosgene ten times more so.

Experience showed that, to be valuable as a war gas, a poison must meet certain requirements. It should be a liquid or be easily liquefied, or it might be a solid, though the solids did not prove as effective as liquids. It must be readily volatilized at ordinary temperatures, and the vapor must have sufficient density to remain near the ground and to maintain its concentration for some time. It must be fairly stable in the presence of moisture and under the molecular shock of the detonating charge of the shell. In addition, it must compare favorably with the most toxic compounds known to science. Hydrocyanic acid fails as a war gas because of the low density of its vapor and the fact that the human organism can withstand the gas below certain concentrations without apparent injury. To kill, then, it requires a concentration which it is not practicable to obtain in the field. Gases like chlorine or phosgene injure in proportion to the amount encountered, so that, while a lethal concentration may not be attained at a given point, nevertheless they will cause casualties of greater or lesser extent, depending upon the concentration and time of exposure.

ORGANIC HALOGEN DERIVATIVES

The second outstanding feature of the war gases is the fact that they are practically all organic halogen derivatives. With the exception of hydrocyanic acid, acrolein, and a very few others, all of the gases which appeared to be of even possible value in the field contain chlorine, bromine, iodine, or fluorine in organic combination. The organic groupings impart the necessary volatility;

the halogens give added weight to the molecule, increasing the vapor density, in many cases giving an instability in the presence of water sufficient to account for the final toxicity. The organic groups also give to a large number of the war gases their characteristic lipid solubility. Of the three or four most effective compounds used, all are soluble in alcohol, acetone, fats, and oils, and so are able to penetrate the cells of the body with the facility of the anesthetics and for the same reason.

SPECIFICITY

The third outstanding feature of the war gases is their specificity. This is more apparent than real, perhaps, but it is sufficiently striking to allow of a rough classification based on the physiological attack. All the gases are irritating to all tissues with which they come in sufficient contact, but under field conditions certain tissues and organs are more quickly or obviously injured by a given gas than are others.

I. *Eye irritants:*

1. Brombenzyl cyanide.
2. Benzyl bromide.
3. Bromacetone.
4. Chloracetophenone.
5. Chloropicrin.
6. Xylol bromide.
7. Dichlorethylsulphide (mustard gas).

II. *Lung irritants:*

1. Chlorine, bromine.
2. Phosgene.
3. Trichlormethylchlorformate.
4. Chloropicrin.
5. Mustard.

III. *Nasal irritants:*

1. Diphenylchlorarsine.
2. Mustard.

IV. *Skin irritants:*

1. Mustard.

EYE IRRITANTS

Taking up the groups in their order, the lacrymators, are characterized by their instantaneous effect on the corneal nerves. Sudden contact with a very moderate concentration of a good lacrymator is as painful as a sharp blow on the eyes, and, indeed, feels very much like it. Such a concentration is immediately unbearable, the eyes are kept shut and the lacrymatory glands are stimulated to a copious secretion of tears. At very low concentrations the lacrymators are felt as a slight irritation of the eye, causing frequent winking and increased flow of tears. Such concentrations are not detectable by the nerves of taste or smell, and do not produce irritation of the respiratory tract except after exceedingly long exposure. Some substances, even with prolonged exposures, fail to show injury to the respiratory mechanism, while they are distinctly and immediately felt in the eye. For example, a concentration of chloropicrin which is perceptible to the eye in time will injure the lung epi-

thelium, but several days of continuous exposure are required before there is evidence of the development of lung edema. The effect on the eyes, however, is instantaneous, suggests a physical or a molecular effect, and is a striking example of specificity. The time element precludes the possibility of hydrolysis or other decomposition, and suggests that this compound is itself a protoplasmic poison with a particular chemical relation to the compounds of the corneal nerve filaments, so that these are stimulated long before other nerve endings or other types of tissue cells are affected. After prolonged exposure, recognizable only in the eye, the respiratory mucosa shows definite injury, and rhinitis, bronchitis, pneumonia, and lung edema develop. At a still later period the kidney also shows injury. Chloropierin is evidently toxic, therefore, to many tissues. As is well known, it is quite stable chemically, and hydrolyzes only very slowly in water. It is soluble in the fat solvents and the fats. Like chloroform, it is picked up by the blood stream from the lungs, and because of a certain degree of tissue specificity it reaches and damages the kidney more perceptibly than the liver, muscles, nerve cells, or other types of tissues. In this it resembles its chemical relative, chloroform, whose specific action on the liver is well known.

Mustard gas, on the other hand, produces no instantaneous effect on the eye. The individual is usually entirely unaware of its presence unless he detects its odor and recognizes it. Hours after exposure the typical injury to the exposed corneal area appears, with conjunctivitis. There is nothing resembling the instantaneous action of the true lacrymators. It may be concluded that mustard gas has no special affinity for the corneal nerve filaments, and that it is not, itself, in the same sense or degree as are chlorine and chloropierin, a protoplasmic poison.

LUNG IRRITANTS

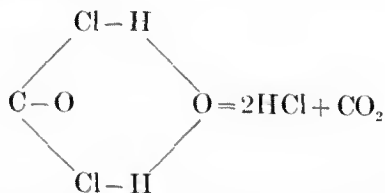
A large number of casualties and some the most severe injuries produced by the war gases are to be credited to the lung irritants.

Chlorine is interesting chiefly because of its historic position as the first war gas used, and because of the dramatic sufferings of the first, unprotected, victims. It is a highly reactive element, combining with protoplasm in a very great variety of ways, irritating and killing tissues, therefore, wherever it comes in contact with it. Chlorine gives evidence of instantaneous reactivity along the respiratory tract and in the eyes. Its effect on the nerve endings of the upper respiratory tract is so intense that in high concentrations it causes immediate spasms of the glottis or violent coughing and vomiting. The lungs later develop the usual reaction to injury of the lining epithelium, namely, edema and necrosis.

Chlorine may replace hydrogen in its organic combinations, incidentally producing hydrochloric acid; it may add directly on to unsaturated molecules or form more stable compounds; it may remove hydrogen from water, causing destructive oxidations, with the formation of hydrochloric acid; it may remove metallic ions from protein combination and thus alter the distribution of electric charges and so change the physical properties of the protoplasm; it may combine with the basic organic groups. These are some of the more obvious ways in which chlorine reacts with and alters protoplasm. These alterations are probably irreversible, chemically or physically, and any such change is assumed to be injurious or, if extensive enough, fatal.

The action of chloropicrin on the respiratory tract has already been touched upon. At moderate concentrations it produces lung edema, intense irritation of the whole tract, violent coughing, and retching. The edema comes on with considerable delay after exposure. Chloropicrin hydrolyzes very slowly in water, so that its effect on the respiratory mucosa can hardly be attributed to a production of hydrochloric acid within the cells, though this factor may contribute in the delayed action. A very general injury to the whole organism is suggested in the fact that men exposed to this gas are described as aging quickly, though the kidney lesions may account for part of this general deterioration. Nothing at all definite is known concerning the chemical action of this gas on protoplasm.

Phosgene and its relative, superpalite, are the most effective of the lung-irritant group. Phosgene is quite reactive chemically. It dissolves and quickly hydrolyzes in water thus:



It is readily soluble in oils and fats and the fat solvents. While phosgene may react in a large number of ways, its lipid solubility and its production of acid in contact with water would appear to be sufficient to account for its great toxicity. The former carries it into the cells like an anesthetic, the latter breaks it up when inside them, with the production of acidity. There is no strong evidence that it is immediately toxic. It produces no striking irritation of the corneal nerves nor, at medium concentrations, of those in the respiratory tract. Diluted, it may be inhaled without discomfort and has, at such times, a rather pleasant odor reminiscent of muscat grapes or of fermenting cornstalks. In more concentrated form the gas produces a sense of shock and a gripping of the chest, but even this immediate sensation passes off and leaves no well-defined sense of injury. Some time later the developing injury to the lung tissues and the resulting edema become sufficient to make the patient aware of his condition, and the feeling of malaise rapidly intensifies. Phosgene itself probably gets as far as the lung capillaries. The packing of the corpuscles in these capillaries during the early stages of phosgene gassing has been established and is probably due to the production of acid in the corpuscle membranes. There is no evidence of action to a greater distance, and from the rate of hydrolysis of phosgene it is improbable on theoretical grounds.

Superpalite behaves like phosgene but is still more toxic.

Mustard gas must be classed as a lung irritant. It has no immediate effect but, like phosgene, is absorbed and hydrolyzes within the cell to produce an acid. It produces, however, a type of reaction in the respiratory tract quite different from that of phosgene, with the formation of a tenacious membrane in the upper portion of the trachea and bronchial tree instead of the excessive edema of the alveoli.

NASAL IRRITANTS

The nasal irritants, as a rule, are not, strictly speaking, gases. They are solids which are highly dispersed in the form of smokes, and which are therefore more apt to collect in the upper respiratory passages rather than in the alveoli. Sufficient concentration or deep breathing incident to heavy work, however, will carry the particles into the deeper portions of the respiratory tract. The phenylchlorarsines are the typical examples of this group. These compounds irritate the nerve endings in the nose and throat, producing violent sneezing or vomiting and coughing. The mode of action of these smokes is not known definitely, though they are probably protoplasmic poisons *per se*, and on decomposition yield phenyl and arsenic groups as well as acid. The fact that they are not gaseous prevents their affecting tissues to any large extent and so limits their field of importance. They can be rather easily removed from the inspired air by a filtering device attached to the mask.

SKIN IRRITANTS

Next to the lung irritants the skin irritants have proved most effective.

Of these, mustard gas $\left(\begin{array}{c} \text{H H H H} \\ \text{dichlorethylsulphide, Cl-C-C-S-C-C-Cl} \\ \text{H H H H} \end{array} \right)$ is typical.

It acts on all the tissues with which it comes in contact—eyes, respiratory tract, and skin. It is a heavy, oily liquid, volatilizing slowly. It dissolves in the ordinary fat solvents, fats, and lipoids, but only to a very small extent in water. It penetrates the cells with considerable rapidity and by virtue of its lipid solubility, tends to collect in the fat droplets and lipoids of the cell. In the watery phase of the cell it hydrolyzes to produce hydrochloric acid. The passage from oil solution to water solution, and finally to hydrochloric acid, is slow and may continue for several days in the cells of a tissue exposed to mustard gas. This leads to a slowly developing injury to skin, eye, and respiratory tract, which increases in intensity, at times, for a period of two to three days and is then followed by the removal of the necrotic tissue and the very slow process of repair. There is very little evidence that mustard gas owes its tremendous toxicity to anything more than its ability to penetrate cells and there to produce acidity. Mustard gas has no immediate irritating action on nerve endings or tissues. Its toxicity develops slowly and is presumably the result of its decomposition products. One of these is hydrochloric acid, and while it is quite possible that other toxic fragments are developed in its breakdown, the acid alone can easily account for much of the injury. One of its hydrolytic products, dihydroxyethyl sulphide, has been shown by Marshall to be practically nontoxic.

In concluding this chapter it seems appropriate to emphasize again the injury which results from the development of acidity within cells. Aside from the well-known action of phosphorus and perhaps chloroform on the liver cells, few clean-cut examples of this type of reaction had been described prior to the war. It may prove, however, that many types of cell intoxicants owe their action to an indirect development of acidity, which becomes the immediate cause of the injury.

There is considerable evidence to show that acid outside of the cell does very little harm. For example, very large amounts of hydrochloric acid

may be injected into the veins of an animal without producing noticeable physiological effects. In this case the acidity is immediately taken care of by the effective buffer system of the circulating medium and the injected acid never reaches the interior of the tissue cells. The mucosa of the stomach is regularly bathed with 0.2 to 0.4 per cent hydrochloric acid, with a hydrogen ion concentration sufficient to indicate with Congo Red, but without damage to the mucosa cells. The neutrality of the cell interior is maintained by the impermeability of its membranes to acid. In the same way the skin resists damage from dilute acids for long periods.

On the other hand, the appearance of acidity within the cell instantly sets in motion the autolytic machinery of the cell, and in direct proportion to the amount of acid developed. Cell proteins are not digested by the cell proteases in the normal reaction of its fluids. When this reaction shifts toward the acid side these proteins become digestible by the enzymes always present. The more acid produced the more protein is rendered available for digestion. These available proteins liquefy and digest away, the structure of the cell is obliterated, the products diffuse out and are transported elsewhere by the blood and lymph, and the cell shrinks or dies and is completely autolyzed. All tissues which have been studied behave in this way toward acidity, but they differ very markedly in the extent of the reaction. Muscle and connective tissues are only slightly digested by their own enzymes, even under the most favorable conditions. They contain relatively large proportions of stroma or skeletal proteins which are not rendered digestible by a physiological or pathological rise in the hydrogen ion concentration. The epithelial tissues, on the other hand, are exceedingly sensitive to increased hydrogen ion concentration. They respond by very rapid and complete autolysis to the optimum increase of acidity. Anything, therefore, which can reach and penetrate epithelial structures and produce acidity within these tissue cells will do the maximum amount of tissue injury. If injury is done to a particularly vital gland or structure, the conditions are right for the maximum disablement of the organism as a whole.

Phosgene, superpalite, and "mustard" combine the properties of the anesthetics with rapid hydrolysis to acids. By the strategy of the war they were applied directly to epithelial tissues. With phosgene and superpalite contact is made with the alveolar epithelium, a vital link in the fundamental functions of tissue respiration. Injury to it is like injury to the heart or blood vessels or the blood. It makes precarious the maintenance of the proper oxygen supply to the body as a whole. With mustard gas the skin epithelium is injured, or the upper respiratory tract. While the former injury is not necessarily fatal unless of large extent, it effectually eliminates the man from active service until the wounds are healed.

When such a combination is effected—of a penetrating, acid-forming substance coming in contact with epithelial organs—there is a lethal toxicity quite equal to that of hydrocyanic acid and, in addition, injuries grading all the way down to zero, in proportion to the amount of gas received by the epithelium. In spite of its chemical reactivity, chlorine has only a tenth the toxic power of these gases (phosgene, superpalite, and "mustard") because it penetrates only slightly, and in the many combinations which it makes with protoplasm only a few lead to the production of acid.

CHAPTER VI

PATHOLOGICAL ACTION OF WAR GASES

GENERAL CONSIDERATIONS

The purpose of this chapter is to describe the anatomical lesions caused by the poisonous gases as they were actually observed and to present the detailed records of 107 autopsy protocols. The general description of the pathology is based chiefly upon these protocols, although advantage has been taken of experimental data to supplement the description of the skin lesions caused by mustard gas and to consider the possible effect of this agent upon the blood and blood-forming tissues.

Without questioning the fundamental importance of the work done upon animals in establishing the general mode of action of the different gases, it is advisable to point out again the difficulties in applying the knowledge thus gained to the human material.

To begin with, the experimental worker knew the gas that was being used, its concentration, at least approximately, the duration of exposure, and the manner of application, whether by contact or inhalation. The pathologist in the field had to rely upon uncertain evidence in regard to the nature of the gas; in many cases no information of any sort was obtainable. There was always the possibility, too, that the subject had been exposed to more than one kind of gas. As to the concentration and length of exposure, it was only in exceptional cases that even a crude and approximate estimate could be hazarded from the history of the case, as, for instance, where a shell burst at the door of a dugout, and it might be inferred that the inmate had been subjected to a very high concentration for a brief period.

There were other complications which made the interpretation of the cases very difficult. Frequently the soldier was severely injured by the very gas shell which poisoned him, or he may have been gassed as he was lying wounded by another projectile. In either event, the traumatic injuries complicated the picture. For example, it was not possible to distinguish between the terminal pneumonia which is always present in patients dying from infected wounds and the secondary pneumonia consequent upon the gassing.

The most difficult problem of all for the pathologist was to distinguish between the direct effect of the gas and the lesions caused by the secondary or supervening infection of the respiratory tract. Many of the gas casualties occurred during the months of October and November, when the pandemic of influenza was at its height amongst our troops.¹ There will be pointed out in detail, later, the extraordinary resemblance between the respiratory lesions in this disease and those caused by certain of the irritant gases, notably mustard gas—a resemblance which extends to the finest histological detail and which is of considerable interest. Here will be indicated the possible interpretations which often arose in such a case. Were the lesions due to the gas alone? Had an influenzal infection followed upon the injury caused by the gas? Was it certain

at all that the patient had initial gas lesions of the respiratory tract, and could he not simply have acquired an influenzal pneumonia while he was in the hospital being treated for skin burns? The last possibility is indicated in some of our cases in which the respiratory complications developed long after the gassing, but is equally possible in some of the more acute cases in which death ensued.

The experimental work upon animals seemed to establish a clear-cut distinction between such gases as have a vesicant or irritant effect upon the skin and upper respiratory passages, and gases of the edema-producing or suffocant type, such as phosgene and diphosgene, whose action is manifest only upon the parenchyma of the lung and which are without obvious effect upon the upper respiratory epithelium. In the majority of the human cases sufficient data are at hand to permit at least of this general differentiation in regard to the type of gas concerned. In individual cases, however, the matter is not so simple. Extensive pulmonary edema, whether as a result of the gas itself or of the succeeding pneumonia (particularly in the influenzal cases), or as a terminal event associated with the failing circulation, was of common occurrence. In the absence of precise clinical data, and of characteristic changes in the skin, eyes, and upper respiratory tract, the diagnosis might remain uncertain. It was particularly difficult to decide in such cases whether the subject might not have been exposed to a suffocant gas in addition to mustard gas.

PATHOLOGICAL CHANGES PRODUCED BY GASES OF THE SUFFOCANT TYPE

In the series of 107 completely studied cases only 4 may with probability be ascribed to poisoning with this type of gas (Cases 1, 2, 3, 4). Death occurred in all of these cases in 3 days or less after gassing. In addition 2 other cases are ascribed to phosgene in the records, but in these the evidence in support of the diagnosis seems inconclusive (Cases 78, 104). The first of these (Case 78) died 14 days, the other (Case 104) 72 days, after the alleged exposure to phosgene. The difficulties in interpreting these cases will be evident on reference to the detailed protocols and need not be discussed here.

This material is inadequate for a full consideration of the pathology and especially for a study of the late or residual lesions which, on experimental and clinical grounds, may reasonably be expected to follow the inhalation of gases of the suffocant type. The discussion, therefore, is limited to a brief description of a typical acute case. Through the courtesy of the French G. A. C. the writer of this chapter had the opportunity to witness several autopsies upon French soldiers and to study the large collection of histological preparations in the laboratory of Professor Mayer at the Collège de France, and the following account is based in part upon these experiences, in addition to the records of the series appended and the references in the literature. Reference is made, also, to the observations of Wilder on his series of 50 necropsies of phosgene cases, in which he states:²

All of these patients had passed through the initial suffocative stage of the intoxication and had died one hour or several hours later. Cyanosis was conspicuous in all. In some cases the skin was an ashy gray, in others it was distinctly violaceous. In all cases the blood in the veins was of a deep chocolate color and very thick. The mouth and nose were usually filled and covered with an accumulation of frothy serous fluid. The lungs were greatly distended and very heavy; they completely filled the thoracic cavity and showed definite

imprints of the ribs. The pleural cavities in bodies examined immediately after death contained from 100 c. c. to 1,000 c. c. of a thin serous or serosanguineous exudate. The surfaces of the lungs were mottled with areas of subpleural emphysema. Cut surfaces of the lungs were extremely wet and bloody from edema and passive hyperemia. The trachea and larger bronchi were filled with foamy serous or serosanguineous fluid, and pressure on the lungs caused this to flow abundantly. The larynx, trachea, and bronchi were moderately hyperemic but presented no edema, erosion, or ecchymosis.

In those cases in which death was delayed for two or three days the edema was less homogeneous, hyperemia was more extensive, particularly at the bases of the lungs, and zones of emphysema occurred at the apices and at the anterior margins. There was also some atelectasis, and if secondary infection had occurred nodules of pulmonic consolidation were in evidence.

Histologically the edematous material seemed to consist of liquid and the debris of epithelial cells. Leucocytes and erythrocytes occurred in late cases only. The cells of the alveolar walls and those of the terminal bronchi appeared swollen and indistinctly outlined, their nuclei staining poorly. Many alveolar capillaries appeared thrombosed and other capillaries were engorged. Still others appeared to be collapsed.

GROSS LESIONS

There was a dusky, livid hue to the lips, ears, finger tips, and dependent portions of the body. Thin, blood-stained fluid flowed from the mouth and nostrils, or a mushroom of foam (*champignon d'écume*) projected from the lips. The opened thorax showed the lungs bulky, meeting in the median line, with very little tendency to collapse when the air was admitted to the chest. They completely filled the pleural cavities, and often showed the imprint of the ribs. The pleural cavities almost always contained several hundred cubic centimeters of blood-tinged serous fluid. The visceral pleura was under great tension, moist, and dotted with petechial hemorrhages or larger reddish splotches. The color was strikingly variegated, pale pink areas of emphysema alternating with dark red firmer patches or even lobes of atelectasis and hemorrhagic edema. The interlobular septa were wide and translucent from edema. The lung weight was greatly increased, often to 900 or 1,000 grams or even more. It offered a tense, doughy, cushion-like resistance, with a strong tendency to pit on pressure. The lobules were large and clearly defined by the edematous interlobular septa. The trachea and bronchial tree were completely or partially filled with pink fluid and foam and the smaller tubes appeared distended. The mucosa was pink or darker red, velvety, and smooth, and there was no necrosis, ulceration, or membrane formation. The sectioned surface of the parenchyma poured forth fluid and foam in great abundance. The alternation of paler, glistening areas, which under the loop were seen to be composed of distended vesicles, with the dark red collapsed regions, inundated with bloody edema, was very characteristic. Some of the cases showed disruptive emphysema beneath the visceral pleura, the air escaping to the subcutaneous tissue about the neck and shoulders.

The blood was thick and very dark in color, but its coagulability was apparently unchanged. Thromboses have been described in the vessels of the lung and elsewhere but were not present in any of the cases of the series. The right chambers of the heart were usually greatly dilated and full of soft very dark cruor. Petechial hemorrhages were seen in the epicardium, in the sheaths of the great vessels, and in the gastrointestinal mucosa. The remaining organs, apart from very intense venous congestion, showed nothing abnormal.

No opportunity was presented for study of the central nervous system. Ricker showed that petechial hemorrhages were found in experimentally gassed animals.³

MICROSCOPIC LESIONS

In the early cases the edematous fluid in the alveoli appeared in the sections as a uniform pink staining material or as a granular or shreddy coagulum. (Fig. 2.) There was little or no stainable fibrin. The capillaries were congested and protruded in a tortuous manner into the lumen of the air spaces.

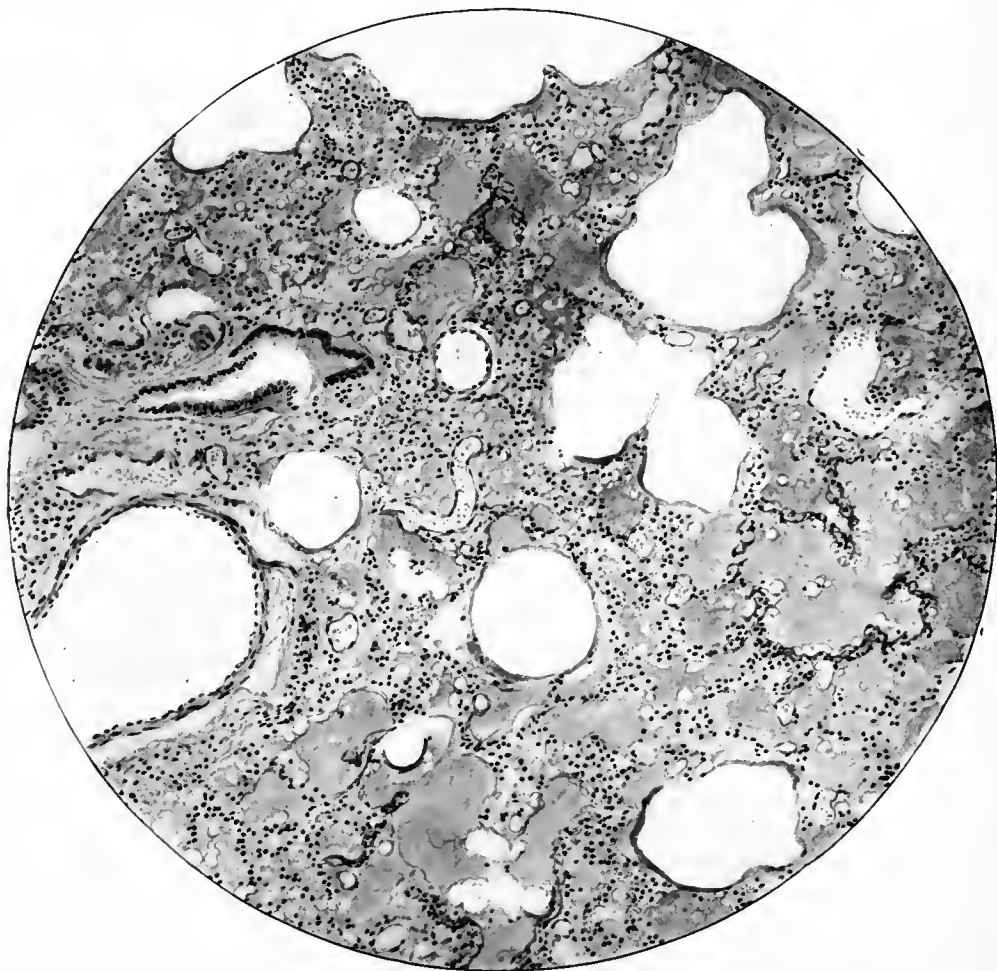


FIG. 2.—Case 2. Lung. Poisoning with phosgene and blue cross gas. Intense alveolar edema, dilatation of alveoli, stasis of leucocytes in capillaries. Epithelium of small bronchi is intact

The preparations studied showed no clear evidence of thrombus formation, due to agglutination of red blood cells, to ante-mortem fibrin deposition or to the agglomeration of platelets in the pulmonary capillaries. Wilder,² however, refers to the occurrence of thrombi, and the experimental findings of Dunn⁴ upon the impermeability of the pulmonary capillaries to injection of saline and carmine gelatine, and the observations of Meek and Eyster⁵ upon the agglutination of red corpuscles in vitro when phosgene is bubbled through a suspension, make it seem possible that the obstruction to the pul-

monary circulation was not due merely to stasis but to an actual clumping of the cells under the direct influence of gas. In addition to the intense edema and congestion there was diapedesis of red blood cells, and, in some areas, more extensive alveolar hemorrhage. The alveolar epithelium was exfoliated and in many of the air spaces the capillaries appeared to lie exposed. There was usually an abnormal number of leucocytes in the blood vessels, a few of which emigrated into the alveoli and septal spaces.

Their nuclei were caryorrhectic. The epithelium of the small bronchi might be lifted up by the underlying edema and partly exfoliated. The peribronchial, perivascular, and subpleural lymphatics were distended, usually with a granular or partly fibrinous coagulum. In view of the statement and the currently accepted belief, based upon animal experiment, that the epithelium of the upper respiratory passages is uninjured by phosgene and diphosgene, it was rather surprising to find that in three cases of the series the tracheal epithelium

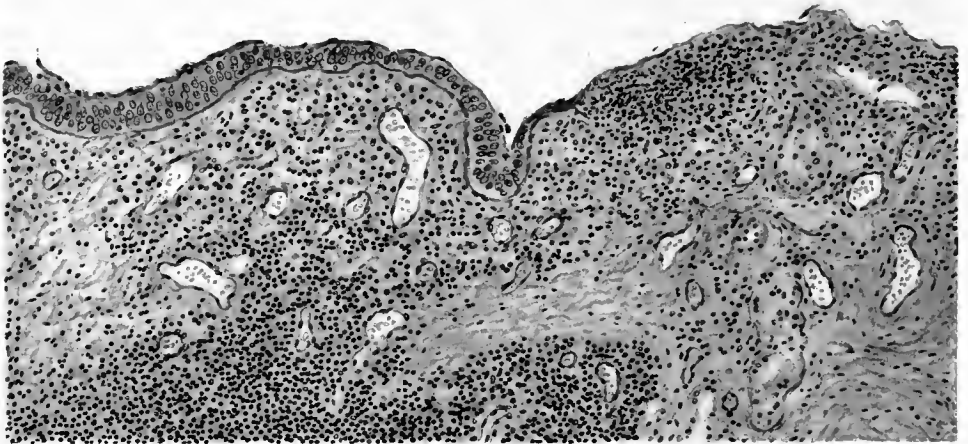


FIG. 3.—Case 2. Large bronchus. The epithelium is in part lost, in part altered, the superficial cells being non-ciliated, and showing hyaline degeneration. There is marked congestion of the capillaries of the submucosa

showed a definite lesion. In two of these cases the superficial cells were hyalinized, the ciliated border was destroyed, and there were signs of nuclear degeneration. (Fig. 3.) Ricker has reported similar lesions of the bronchial epithelium in cats exposed to high concentrations of phosgene in the gassing chamber.³ In the third case there were in addition definite erosions, with local inflammatory reaction. Whether these lesions were due to the phosgene or diphosgene alone or, as seems more probable, to the admixture of more irritant gases, such as chloropicrin or diphenylchlorarsine, or whether they were the result of the early bacterial invasion, can not be decided from the study of the very limited material. In one of the cases (Case 3) there had already occurred, after 24 hours, a very massive invasion of streptococci in both trachea and lungs.

In the other viscera lesions were not found which could with any degree of probability be attributed to the gassing. The intense venous congestion found in the gross was evident also, of course, in the sections. Parenchymatous

changes in liver and kidney may be ascribed to the concurrent infection rather than to a direct toxic action of the gas upon these viscera. There has been general agreement, indeed, that absorption of the gas (phosgene) is unlikely, in view of its rapid decomposition in the presence of water.

PATHOLOGICAL CHANGES PRODUCED BY GASES OF THE VESICANT TYPE (DICHLORETHYLSULPHIDE)

CUTANEOUS LESIONS

The pathology of the skin lesions caused by dichlorethysulphide was very thoroughly studied by Warthin and Weller in this country and by Mayer at the central laboratory of the French medicolegal service at the Collège de France, Paris. The studies recorded here on the human cases coming to autopsy have been supplemented by the examination of pieces of skin excised at varying intervals after the application of mustard gas in alcoholic solution of known strength under standard conditions.

The gross changes which followed the application of this substance may be summarized as erythema, followed by vesication and a variable degree of pigmentation. The vesicles were usually superficial; only rarely was the superficial portion of the corium involved. The customary sites for the burns were the face, especially the scalp, the eyelids, nose and lips, neck, axillæ, elbows and knees (from lying or kneeling on contaminated ground), the under surface of the penis and the contiguous anterior aspect of the scrotum, the inner surface of the thigh, the buttocks, and the hands and feet. (Pls. II, VII, VIII.)

It is now a familiar fact that after exposure there was a definite latent period which varied from a half hour to six or eight hours or even longer. It was not uncommon for small sudaminal-like vesicles to appear in crops at intervals of days after the exposure. In some cases, presumably those exposed to low concentration of the vapor, there was produced a very diffuse, almost scarlatina-form erythema, changing in color from a somewhat dusky pink, through purple, to brownish. In other cases the vesicles were surrounded by an erythematous zone, which later became brownish. The duration of the pigmentation was not definitely known and probably varied in different individuals. Pigment flecks at the site of a small experimental burn were apparent after a year. The contents of the vesicles were usually clear, although the fluid might contain a few filmy fibrin clots. If infection occurred the fluid might become purulent, but ordinarily relatively few leucocytes were found on examination of the fresh fluid. It was frequently reported that a burn over the sacrum had developed into decubital ulcers.

Since deaths usually occurred from the fifth day to the end of the third week after exposure, the pathologist was apt to see only raw surfaces, blebs, ulcers, scars, or pigmentation, rather than erythematous lesions. These were also more apt to be in locations subjected to long friction during travel to the hospitals and thus, to a certain extent, the regional distribution of the burns, when tabulated from autopsy reports, differed from that of the lighter burns sustained by those who recovered.

The earliest lesion examined histologically was excised 3 hours and 25 minutes after the application of a 10 per cent solution of dichlorethysulphide

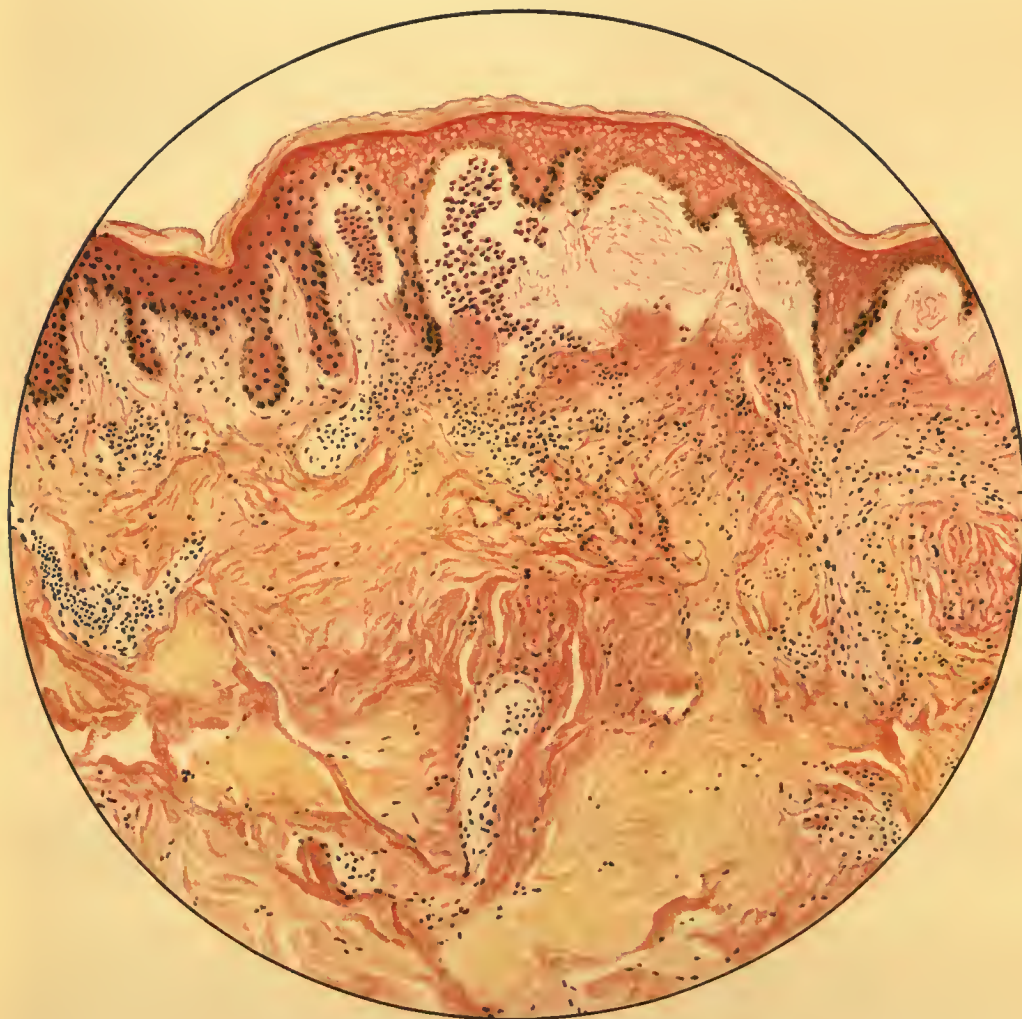


MUSTARD-GAS INHALATION. DIPHTHERITIC INFLAMMATION WITH FORMATION OF FALSE MEMBRANE, UPPER RESPIRATORY TRACT.



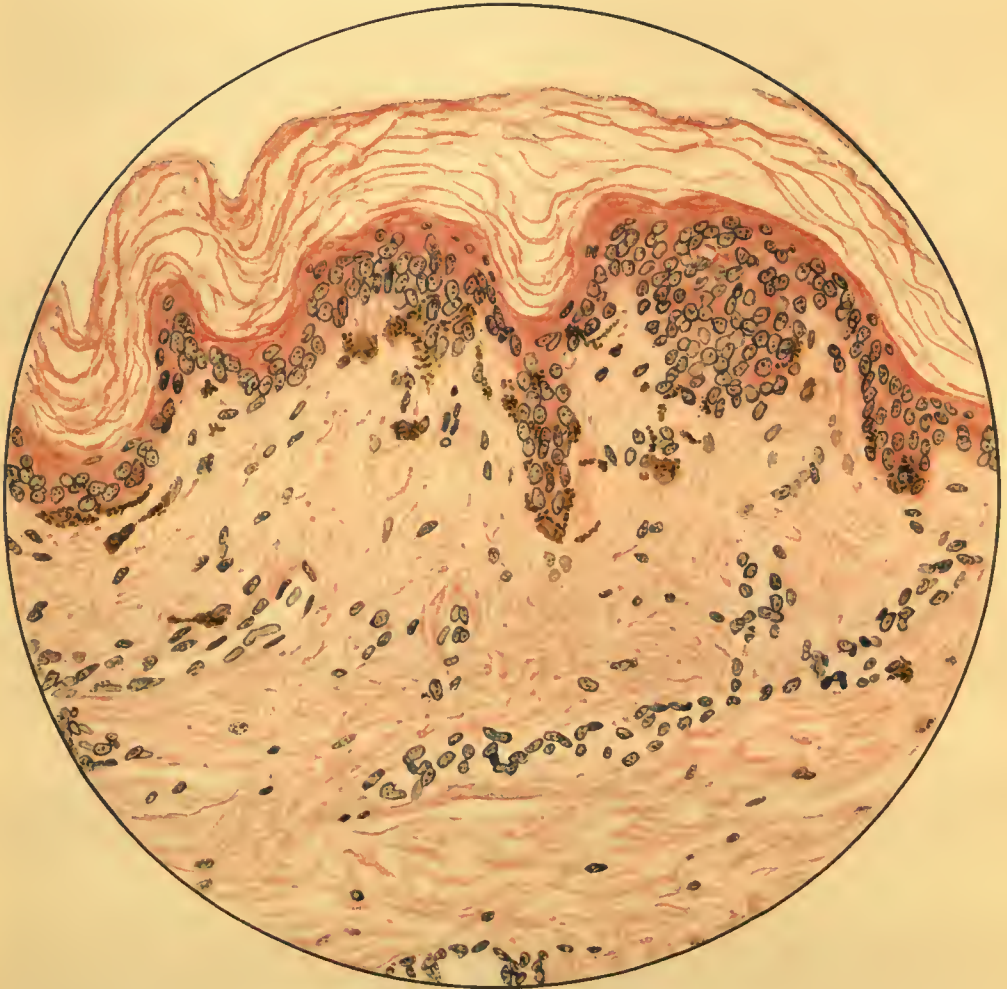
MUSTARD GAS BURNS OF EXTERNAL GENITALS, WITH VESICULATION
AND PIGMENTATION.

Note change in staining of necrotic epidermis and vacuolar degeneration of nuclei at margin of vesicle.



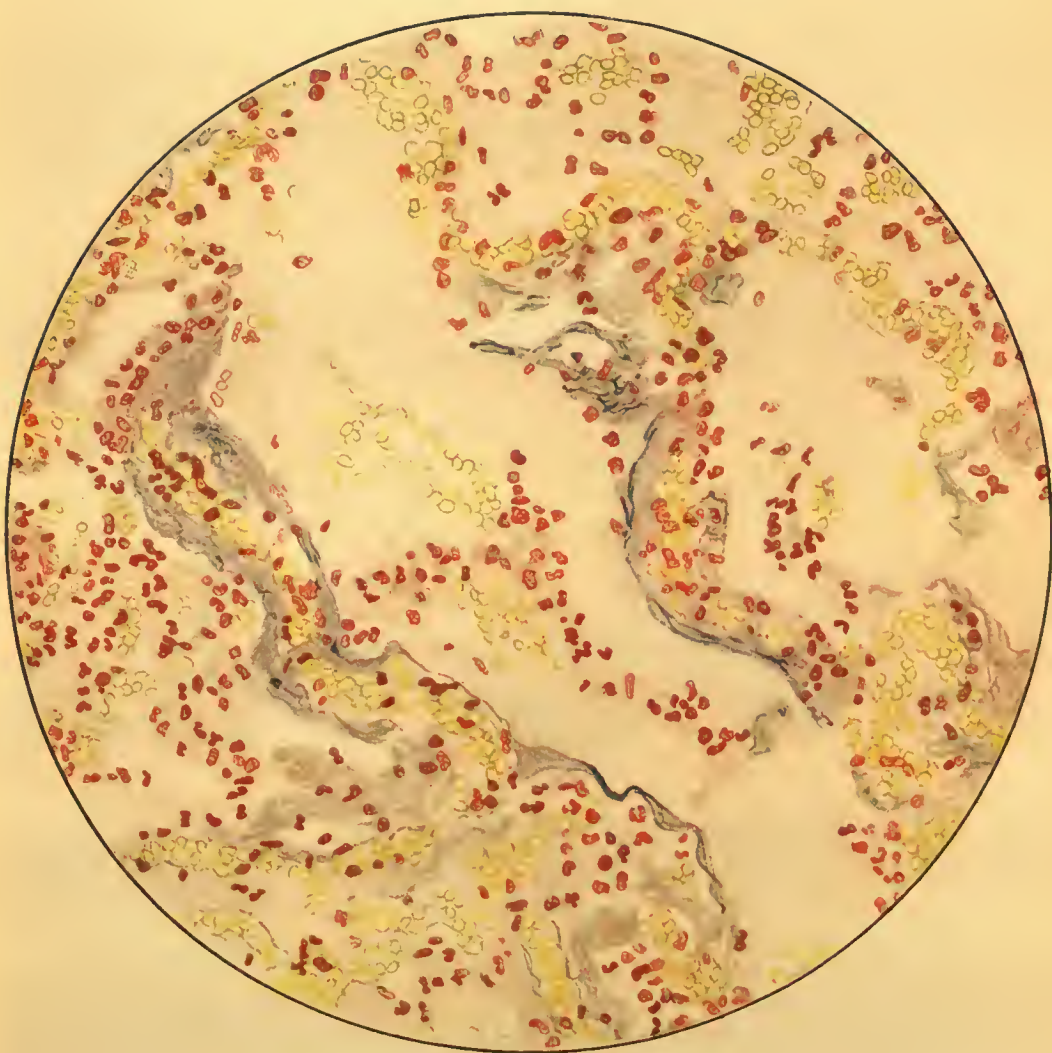
A. POER & CO. LITH. BALTIMORE

EXPERIMENTAL MUSTARD GAS BURNS (NEGRO), 24 HOURS. VESICLE FORMATION, WITH NECROSIS OF OVERLYING EPIDERMIS AND INFLAMMATORY REACTION AT MARGIN OF VESICLE.



A. MOEN & CO. LITH. BALTIMORE

CASE 86. MUSTARD GAS BURN OF SCROTUM, 18 DAYS' DURATION. HYPERKERATOSIS, HYPERPIGMENTATION, WITH IRREGULAR DISTRIBUTION OF PIGMENT, CHROMATOPHORES IN CORIUM.



A. HOBBS & CO. LITH. BALTIMORE

CASE 6. MUSTARD GAS, 2 DAYS. LUNG.

The distended atria are lined with a hyaline band giving an indistinct fibrin reaction with Gram-Weigert Saffranin stain.



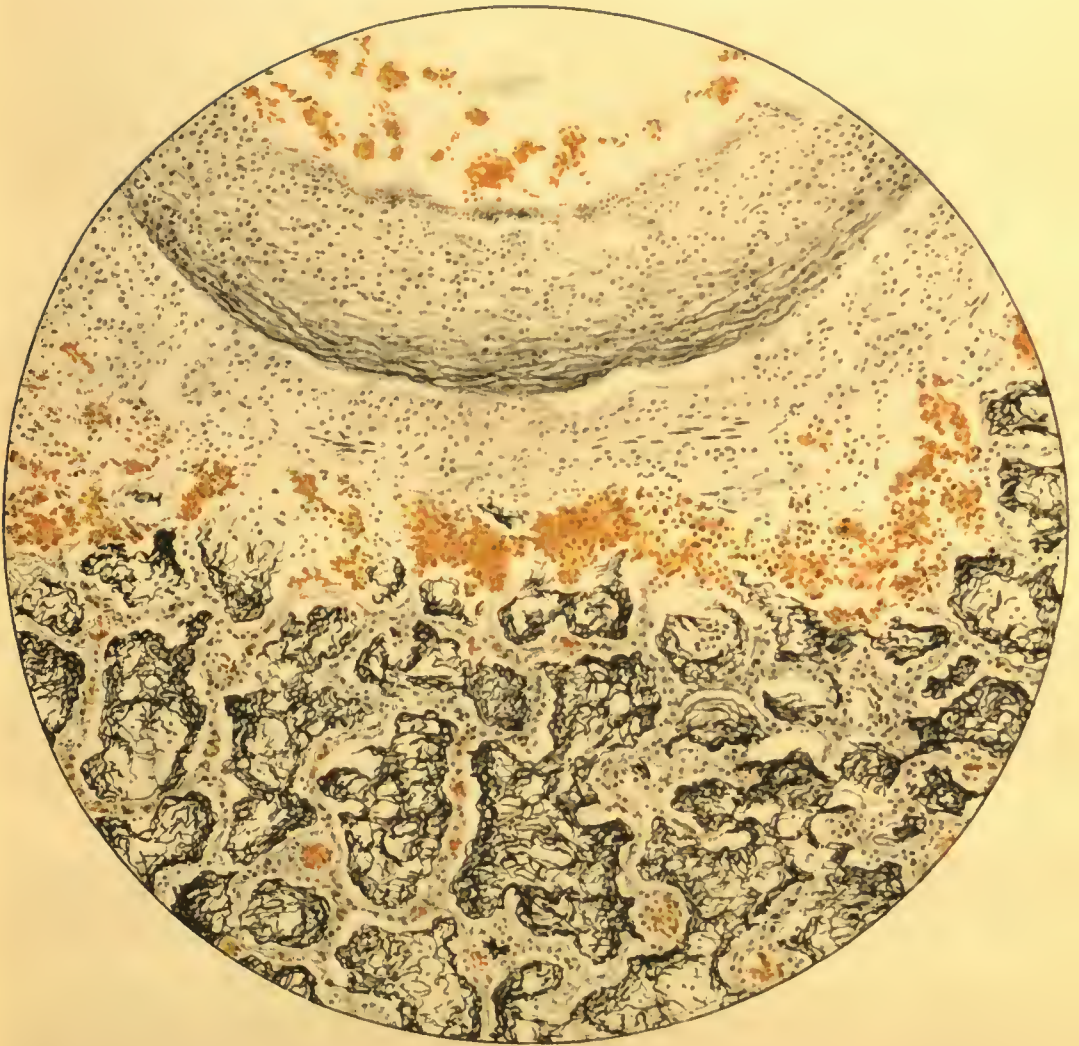
A. HORN & CO. LITH. BALTIMORE

MUSTARD GAS BURN (CONTACT) OF NECK.



A. HEDDER & CO. LITH. & BALTIMORE

MUSTARD GAS BURNS OF BODY.



• HOPKINS & CO. LITH. & BALTIMORE

CASE 24. MUSTARD GAS, 5 DAYS. SECTION THROUGH WALL OF SMALL BRANCHES, SHOWING FALSE MEMBRANE REPLACING THE NECROTIC EPITHELIUM, HEMORRHAGE INTO ADJACENT ALVEOLI, AND FIBRINOUS EXUDATE INTO THE ALVEOLI EXTERNAL TO THE ZONE OF HEMORRHAGE.

(Gram-Weigert Saffranin stain.)



GROSS CHANGES IN LARYNX AND TRACHEA OF A SOLDIER WHO DIED FOUR DAYS AFTER INHALATION OF MUSTARD GAS.

in absolute alcohol, applied for 5 minutes over an area of 1 mm. in diameter in the skin of the back; at the time of excision there was a slightly elevated area of erythema about 3 mm. in diameter.

The only change noted in the epidermis was a slight thinning with a flattening out of the papillary processes; over the summit of the lesion they were completely obliterated. Under the high power a few individual cells showed a vacuolated cytoplasm with displacement of the nucleus to the periphery of the cell. There was slight edema of the corium; the sweat glands, hair follicles, and sebaceous glands showed no recognizable injury; the blood vessels, especially the superficial capillaries, were dilated and filled with red cells and a few were surrounded by a loose mantle of lymphoid cells; the lymphatic vessels were distended, containing a fine granular coagulum; the deeper portion of the corium and the subcutaneous tissue showed no injury.

Another lesion was examined after 45 hours, having been produced at the same time, in the same individual; the lesion consisted of a small elevated vesicle filled with clear fluid and surrounded by an area of erythema 4 to 5 mm. in width.

The overlying superficial horny layer was still intact, but the remainder of the epithelium covering the vesicle was entirely necrotic. The contents of the vesicle consisted of interlacing fibrin strands inclosing a homogeneous coagulum loosely infiltrated with polynuclear leucocytes. At the margin of the vesicle the epithelial cells were dissociated for a short distance but rapidly became normal. No mitoses were found and there was no indication of increased proliferative activity. The base of the vesicle was formed by edematous corium which, in its most superficial portion, was devoid of connective tissue nuclei and was loosely infiltrated with round cells and polynuclear leucocytes. These were most densely aggregated about the blood vessels. The deeper connective tissue showed no edema or inflammatory reaction.

The perivascular infiltration extended for a considerable distance beyond the area of the vesicle; the sweat glands and hair follicles in the vicinity of the lesion showed no significant changes.

Although it would appear from a study of this experimental lesion that the vesicle was formed between the epidermis and the superficial corium, a study of numerous other accidental lesions showed that this was by no means always the case; the vesicle may be formed within the epidermis itself by a dissociation of the epithelial cells with the accumulation of fluid between them and their subsequent necrosis. In this way a cleft may be formed, the epidermis and some of the basal cells remaining visible. (Fig. 4.)

Not only might fluid accumulate between the cells, forcing them apart, but the cells themselves might undergo hydropic changes, so that the cytoplasm would contain a single large vacuole which pushed the nucleus in crescentic form to the periphery of the cell. This type of hydropic degeneration was frequently seen at all stages, especially amongst the less severely injured cells at the periphery of the lesion.

In other cases individual cells, or the entire epidermis, would undergo a hyaline necrosis, the nucleus becoming shrunken and pyknotic and the cytoplasm taking on a dense refractile appearance and staining deeply with eosin. This mummified or hyalinized epidermis, constituting often the cap of the vesicle,

might persist for a long time, showing in a shadowy way the outline of the individual epithelial cells. It might persist until a new growth of epithelium proceeding from the margin of the vesicle had completely undermined it and recovered the base of the vesicle. This was one of the common methods by which regeneration took place. (Fig. 5.) There was no doubt that the sheaths of the hair follicles also played an important part in reinvesting the base of the vesicle or ulcer, although this was even more striking in the lesions experimentally produced in horses.

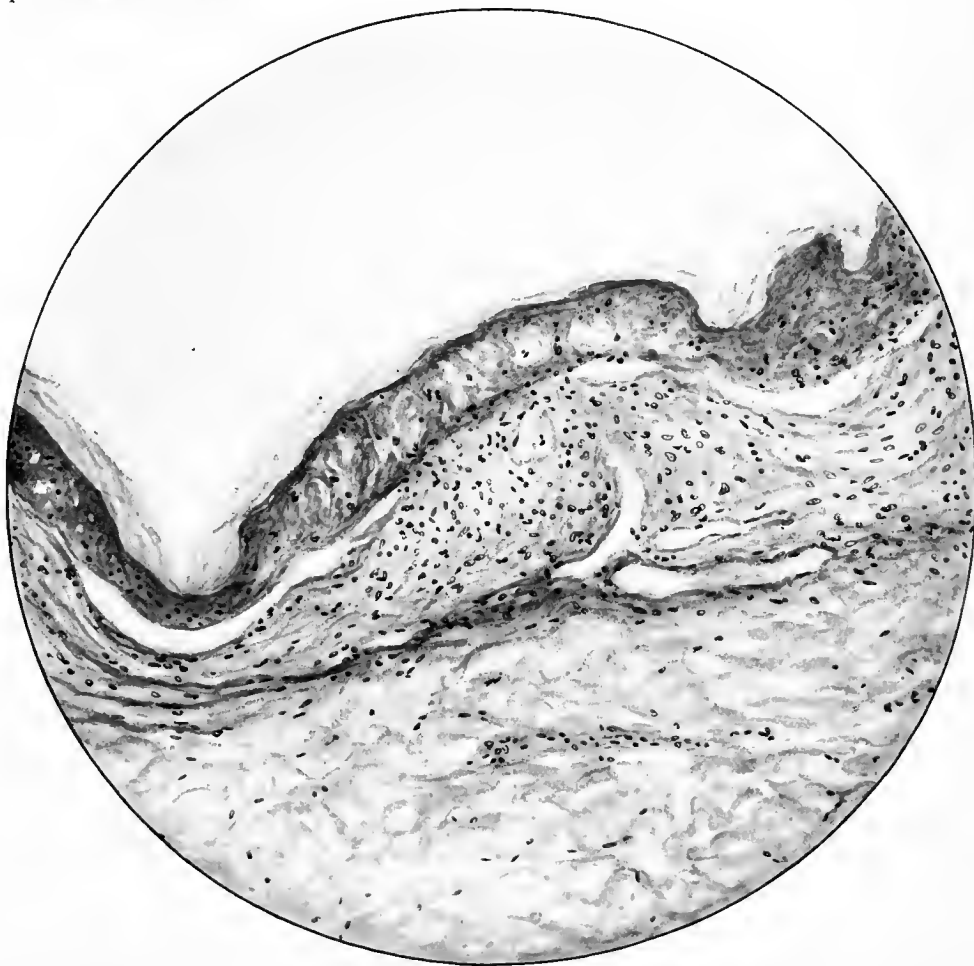


FIG. 4.—Case 8. Mustard-gas burn of skin of 2 days' duration. Necrosis of epidermis, with beginning of intra-epidermal vesicle formation

The opportunity was presented to examine histologically experimental lesions produced in the way indicated above in negroes. Although it has been demonstrated by the studies of Marshall, Lynch, and Smith, cited below (see also Chap. XII), that the negro is relatively insusceptible to dichlorethylsulphide, the lesion produced by a 10 per cent alcoholic solution differed in no respect from the lesions in white individuals. One of the preparations excised after six hours showed very clearly the early edema in the papillary layer of the corium which preceded vesiculation. The tissue was very loose and foamy, and occasionally the entire epidermis was elevated by a granular

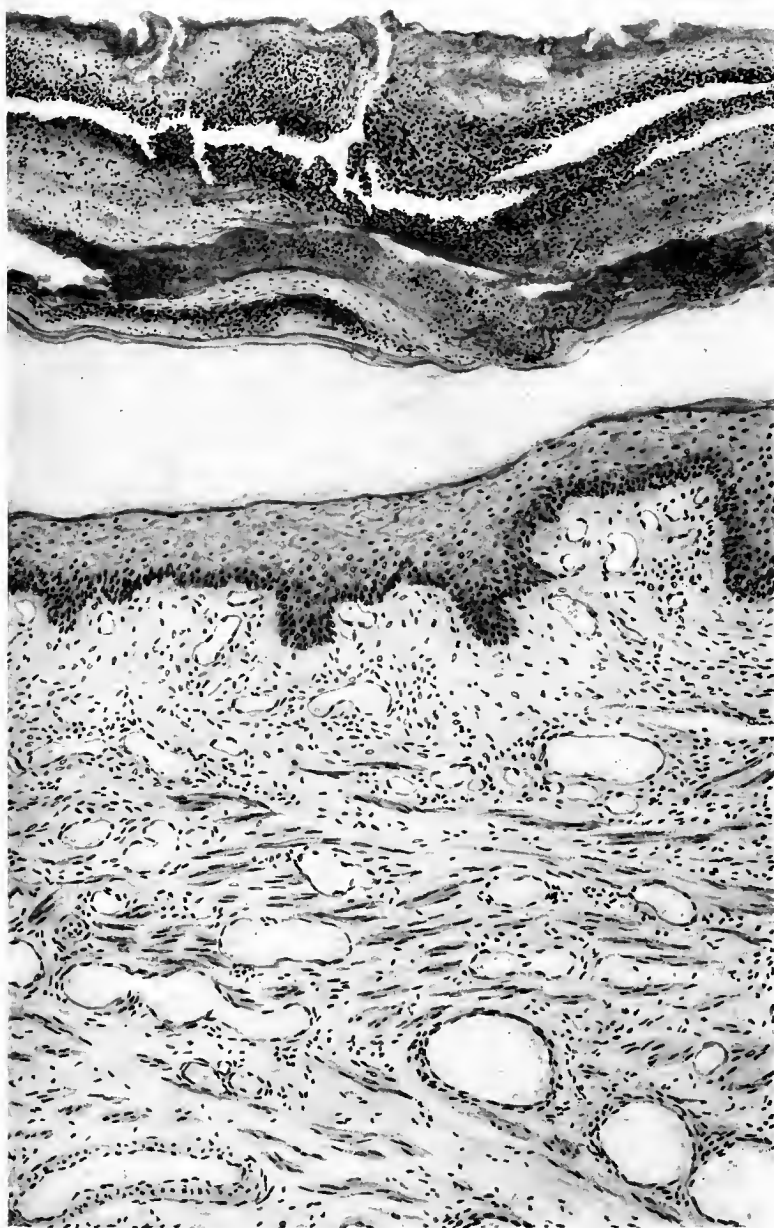


FIG. 5.—Case 89. Mustard-gas burn of 20 days' duration. Regeneration of new epithelium beneath crust of necrotic original epithelium. Hyperemia. Absence of inflammatory reaction

coagulum. The same type of degeneration of the cytoplasm was found in the connective tissue and endothelial nuclei. There was hyperemia and a moderate inflammatory reaction in which polynuclear leucocytes played the leading part. (Pls. III, IV.)

Many of the preparations obtained from autopsy cases showed definite evidence of infection, with the typical inflammatory response. Since these may be regarded as incidental lesions and are in nowise distinctive they need not be considered in detail.



FIG. 6.—Case 18. Mustard-gas burn of 5-6 days' duration. Section through vesicle. Overlying epithelium is necrotic. The contents of the vesicle consist of homogeneous, slightly fibrinous coagulum with moderate numbers of leucocytes. The underlying corium is edematous

The pigmentation which was so striking a feature of the later stages was due to an increased production of melanin pigment by the cells of the rete mucosum and was not to be attributed to the deposition of blood pigment following capillary hemorrhages. The pigment production was often irregular, individual cells being loaded with coarse clumps, while adjacent cells might be wholly pigment free. Moreover, pigment-containing cells could be present in abnormal situations—in the stratum granulosum, for example, or even amongst the cells of the keratin layer. Usually, numerous chromatophores were seen in the capillary layer of the corium. (Pl. V.)

Where the burn had been a severe one, and the subepithelial tissue had been involved, definite fibroblastic growth was found in the later stages. The leucocytes which, in the early stages, were chiefly polymorphonuclear, and which tended to become fragmented as they approached the surface, gave way to lymphoid cells; but at no stage of the process was the cellular reaction, in uninfected cases, a very intense one.

The vascular lesions throughout appeared to be of minor importance. Thrombosis was exceptional, being found only in very severe burns in which there was a direct necrosis of the corium. These findings, therefore, are not



FIG. 7.—Case 18. Another section, showing condition similar to that seen in Fig. 6

in accord with the view of other observers, who hold that the injury to the blood vessels is an important factor in delaying the repair. The persistence of the injury and the retarded healing appeared to be due, rather, to the continued action of the dichlorethylsulphide.

To summarize briefly the lesions produced in the skin: There was caused a hydropic degeneration, or a hyaline necrosis of epidermal cells, often with the formation of vesicles within the epidermis. There was produced, also, edema of the corium beginning in the loose tissue of the papillæ and leading to the separation of the epidermis from the underlying connective tissue and the formation of the vesicle. (Figs. 6 and 7.) There might be produced

in severe burns a direct necrosis of the superficial portion of the *corium*. There was an initial hyperemia and a very moderate acute inflammatory reaction in which polynuclears were the predominant element in the early stages. The leucocytes became pycnotic and fragmented as they approached the surface. A severe injury to the small cutaneous vessels was exceptional and thrombi were rarely found.

Regeneration took place by a growth of new epithelium from the margin of the vesicle, as well as from the sheaths of the hair follicles. If the dead epidermis was not artificially removed, it might remain as a protective covering until healing was completed.

There was an active growth of new connective tissue in the superficial layers of the *corium* where this had been injured. The hyperpigmentation was due to increased melanin production by the cells of the *stratum mucosum*. It was frequently irregular and atypical.

EYE LESIONS

No material was available for the study of the histopathology of eye lesions in human cases. The subject will be considered in Chapter XV of this volume and in Section IV, "Ophthalmology, American Expeditionary Forces," of Part II, Vol. XI.

LESIONS OF THE RESPIRATORY TRACT

It is difficult to describe a typical picture, inasmuch as great variations were encountered in different cases. Appearances depended upon a number of factors—the duration of life after gassing, the concentration of the gas, and the duration of exposure. Most of all did the lesions vary with the character of the secondary infection which invariably followed the original chemical injury. One can not hope, therefore, to depict a graded series of injuries followed by repair. Indeed, the more cases that are studied the more difficult does it become to trace out the direct effects of the poison amidst the havoc wrought by the secondary bacterial invaders, and the more difficult is it to decide whether late changes in the respiratory tract shall be considered as the healing of the chemical injuries or of the infectious lesions.

It is with this reservation, therefore, that the cases are described as they were actually recorded in the case protocols and notes, leaving to the experimental workers the determination of the precise part played by the poison itself and by the bacterial infection in the production of the lesions.

UPPER RESPIRATORY TRACT

Mustard gas in sufficient concentration produced a complete necrosis of the epithelium of the larynx, trachea, and bronchi. It was the rule for the smallest bronchi to be less severely injured, but yet there were many exceptions to this, and in some cases the necrosis extended into the smallest bronchi, infundibula, and, perhaps, although this was more difficult to determine, to the alveolar epithelium itself. The usual gross picture in the early cases was that of a diphtheritic inflammation, with the formation of a false membrane, which began at the epiglottis, or even in the pharynx, and extended more or less continuously to the small bronchi. (Figs. 8 to 11, Pl. I.) The membrane often was firm and tenacious and lined the upper air passages, forming a cast more or less

adherent, or there might be small adherent raised patches covering the eroded and hemorrhagic sub-epithelial tissue. In a few of the cases the membranous inflammation did not involve the trachea itself, but only the larger and medium sized bronchi.

Not all the cases showed this intense diphtheritic necrosis; at times a membrane was entirely lacking, but the mucosa appeared rough and sandy and covered with shreds of fibrinopurulent exudate. It was always hyperemic and often dotted with punctate or larger hemorrhages. In later cases the membrane might be replaced by masses of soft crumbling purulent or bloody exudate.

Careful dissection of the bronchial tree was very apt to show that the membranous casts which completely occluded the middle-sized bronchi as far as the third or fourth branches were replaced in the smallest branches by a softer purulent exudate. Examination of the lining of the bronchus showed a corresponding alteration from a rough hemorrhagic, ulcerated surface to a smoother, merely hyperemic one.

In later stages, when epithelial regeneration had occurred, the membrane or exudate was cleared away, and the surface was smooth, opaque, and thickened. How this regeneration occurred will become apparent in a study of the histological changes, but it may be noted here that even weeks or months after gassing, erosions, more or less localized or diffuse, might persist. This was the case where injury had been so deep-seated as to involve not only the superficial epithelium but also that of the ducts of the mucous glands, so that no possibility of regeneration obtained.



FIG. 8.—Mustard-gas poisoning. False membrane extending from epiglottis through entire trachea into bronchi

In a few of the cases the lesions of the upper respiratory tract were gangrenous rather than diphtheritic in character. (Pl. X.) The walls of the trachea and bronchi showed greenish discoloration, and the exudate had

a characteristic foul odor. There were usually associated gangrenous areas in the lung itself. In two such cases the pathologist recorded the presence of extensive dental caries, indicating that, in his opinion, infection of the air passages had occurred, with the putrefactive bacteria from the mouth. This seemed a plausible idea, and in one of the cases it was supported by the finding of numerous fusiform bacilli in the necrotic exudate. Spirilla were not demonstrated, but were doubtless present.

The histological lesions found in the trachea and bronchi were studied in a severe case, dying two days after exposure. The trachea and large bronchi presented about the same picture. There was a thick, fibrinous membrane with coarse laminated threads running parallel to the surface. In the meshes lay scattered nuclear fragments and a few better preserved wandering cells; masses of mucus, also, sometimes showing a curious concentric arrangement, were incorporated in the fibrinous membrane. Adherent to the under surface were the detached epithelial cells, many of which were surprisingly little altered, still conserving their cilia and showing good nuclear stain. The membrane lay loosely upon the exposed basement membrane, being



FIG. 9.—Diphtheritic necrosis of mucosa of upper respiratory tract after mustard-gas inhalation

attached only here and there by bridges of fibrin. The basement membrane itself was swollen and less sharply outlined than the normal structure. The subepithelial tissue was edematous; in places there was a definite fibrinous exudate between the connective tissue bundles. There was a moderate inflammatory infiltration with both mononuclear and polymorphonuclear leucocytes. As these approached the surface they appeared to undergo caryorrhexis, and in the superficial portion there was much nuclear debris. The nuclei of the connective tissue cells also showed the effects of the injury, their nuclei being shrunken and pyknotic. The blood vessels were enormously distended, and there were small capillary extravasations. The endothelium showed no definite alteration. The mucous ducts were widely distended with plugs of mucus. Near the surface their epithelial cells were apt to be cast off and more or less degenerated. In the deeper portion the cells lost their orderly alignment and tended to take on a squamous type. The mucous glands themselves at this stage were in a state of hypersecretion; only exception-



FIG. 10.—Diphtheritic necrosis of mucosa of upper respiratory tract after mustard-gas inhalation



FIG. 11.—Diphtheritic necrosis of mucosa of upper respiratory tract after mustard-gas inhalation

ally were there clearly defined degenerative changes in the gland cells to indicate a penetration of the poison. The loose cellular tissue about the perichondrium, and even between and external to the cartilages, might be edematous.

In the case described the injury had been limited to the superficial epithelium and had not led to the death of the tissue below the membrana propria. Many of the cases of the series, however, showed a more deep-seated injury, involving the subepithelial tissue to a variable depth. (Figs. 12 and 13.) The basement membrane appeared to offer an obstacle to the penetration of the poison, but when this was overcome the necrosis of the connective tissue frequently extended to the bands of smooth muscle fibers lying superficial to the mucous glands. The muscle fibers again seemed to offer a resistance to the further penetration of the poisonous substance. Only exceptionally was there a direct necrosis of the mucous glands, and even in those cases the destruction involved only groups of acini and not the mucous glands in their entirety.

A well-formed membrane was seen as early as 48 hours after gassing and might persist for many weeks. In cases where no membrane was present the surface of the trachea was formed by the exposed necrotic subepithelial tissue or by the smooth and wavy contour of the basement membrane. (Fig. 14.) In the early stages shreds of epithelium were still to be found here and there, but these were rapidly cast off and replaced by regenerated cells in a manner to be described.

The reparative processes which followed the injury above described were most interesting. As early as four or five days after gassing, a beginning reinvestment of the trachea or bronchus might have taken place. The new cells were derived from little islands of epithelium still adherent to the membrana propria which had escaped the initial destruction and from the epithelial cells which had lined the ducts of the mucous glands. (Fig. 15.) These



FIG. 12.—Mustard-gas burn. Deep-seated necrosis of bronchial mucosa

cells divided and crept out over the mouth of the duct covering the adjacent exposed basement membrane, first with a single layer of flattened cells, later with a multilayered squamous epithelium. These duct cells seemed to play a very important rôle in epithelial regeneration, and it was a common finding to see the entire duct filled with a solid nest of actively dividing cells. In this way, provided the destruction had not been too intense, the entire surface might be reinvested with a metaplastic epithelium of the squamous cell type. (Fig. 16.) Whether the superficial cells of this layer later became replaced by cylindrical ciliated cells can not be definitely stated until opportunity has presented to examine further material from late cases. In one of the cases after 167 days, in which typical mustard gas lesions were still present in the bronchi, the trachea showed a multilayered but ciliated epithelium. The majority of the late cases, however, showed epithelium of the squamous cell type, and it is probable that in most cases the metaplasia was a permanent change.

Certain of the cases showed interesting details in regard to the process of epithelial regeneration. Worth noting is the fact that regeneration might begin while the membrane was still present, so that it was not unusual to find a

layer of flattened cells showing many mitotic figures, often highly atypical in character, interposed between the fibrinous exudate and the basement membrane. Often it seemed as if the epithelial growth had outstripped the other processes of repair, so that the growing cells themselves, because of being improperly nourished, degenerated. (Fig. 17.) Some of the preparations showed the new epithelium lifted up from the membrana propria by a granular coagulum, as if a new vesicle had been formed. This appearance leads one to

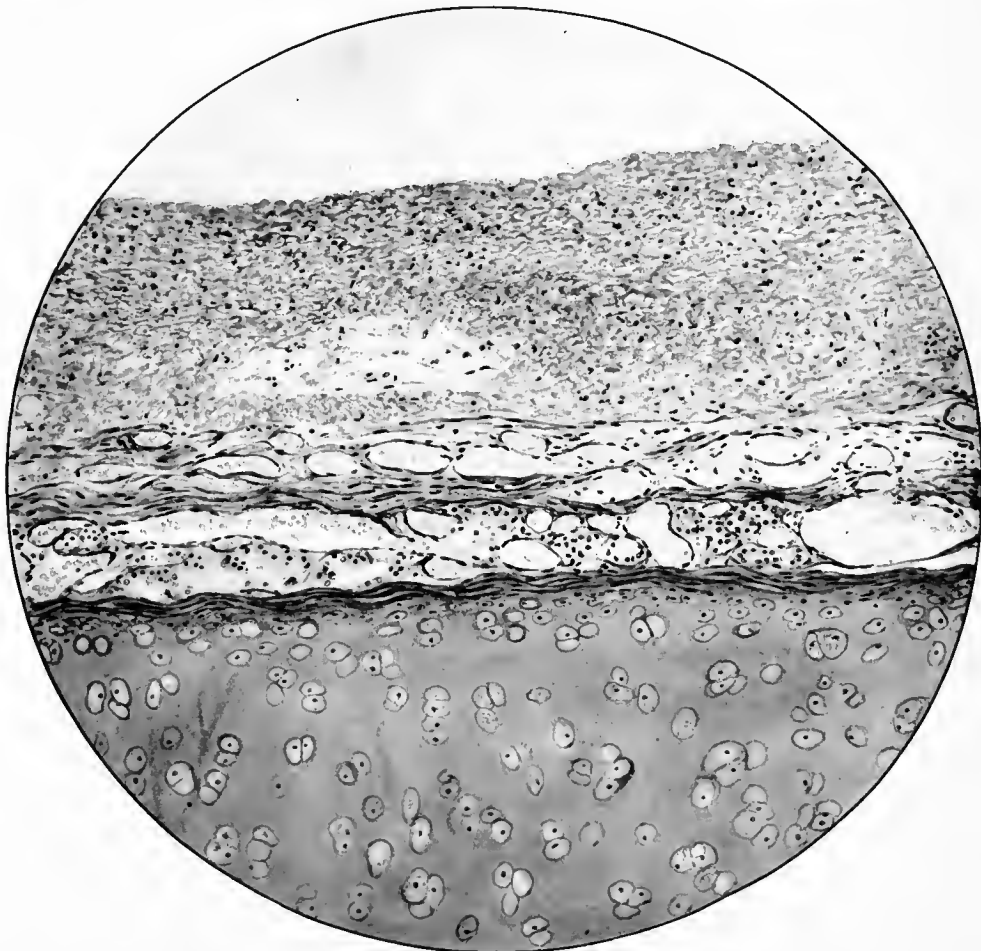


FIG. 13.—Case 22. Mustard-gas burn, 5 days' duration. Deep necrosis of tracheal mucosa

ask whether there may not have been a persistence of the poison and whether this late and secondary vesicle formation may not be comparable to the late appearance of skin vesicles four or five days after gassing.

One of the preparations showed the duct epithelium growing beneath the still preserved basement membrane. (Fig. 18.) This anomalous growth was due to the proliferation of the duct epithelium beneath the partially loosened membrana propria. In one of the late cases, scattered through the sub-epithelial tissue, were solid nests of cells which resembled very closely squamous-celled carcinoma. The cells were arranged as in epitheliomatous pearls; they

were definitely squamous, highly atypical, often multinucleated, and showed numerous mitotic figures. Intracellular fibrils even were to be seen between them. This appearance was brought about by the proliferation of the duct epithelium within the lumen. (Fig. 19.)

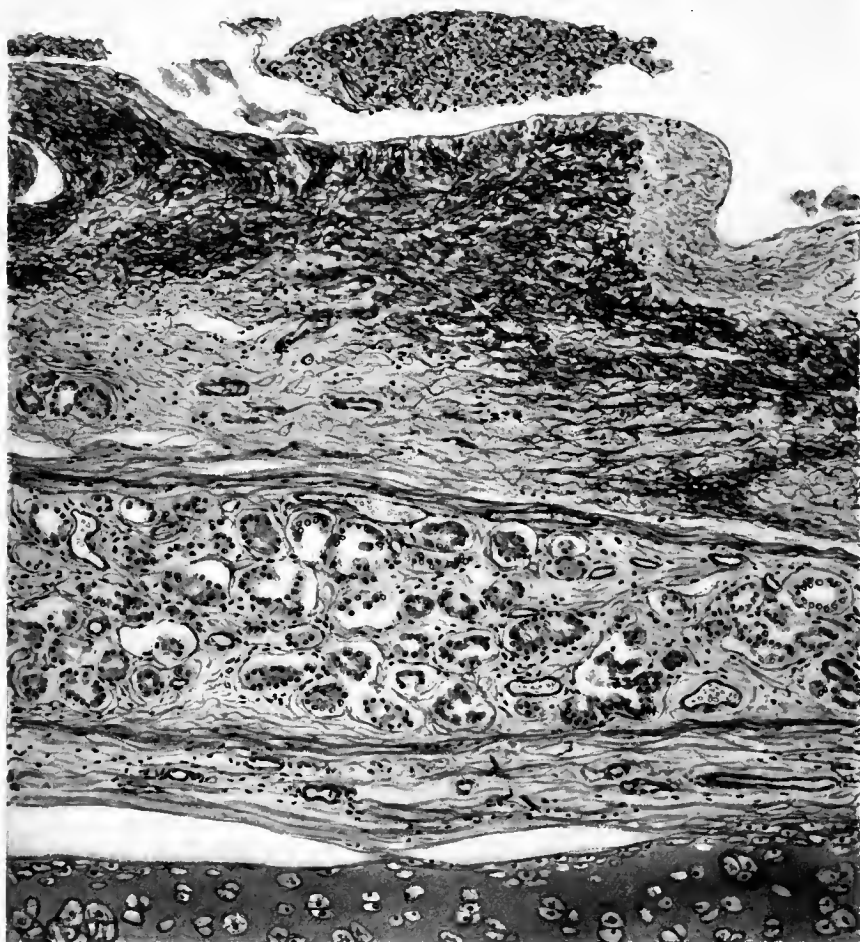


FIG. 14.—Case 21. Mustard-gas burn, 5 days' duration. Necrosis and exfoliation of trachea lepithelium exposing basement membrane. Fibrinous edema of submucosa

As regards the lesions in the submucosa, it has been stated above that in the majority of cases the cellular response was not very marked, and in some cases, in the trachea at least, practically wanting. Bacterial stains showed that the organisms rarely penetrated below the surface. In one of the cases, however, in which there was an extreme edema not only of the submucosa tissue but also of the areolar tissue external to the bronchus, a Gram stain showed unrestrained growth of Gram-positive cocci throughout the edematous area.

With the beginning of repair the connective tissue cells in the submucosa took on the character of fibroblasts. New blood vessels were formed which were sinusoidal in character and which formed wide channels extending to the basement membrane, where this was still intact. The inflammatory cells then became predominately lymphoid in character, and numerous plasma cells and other large mononuclear elements were present. This formation of a very vascular granulation tissue was found not only in the trachea and large bronchi, but in the medium-sized and smaller bronchioles, where it sometimes led to a

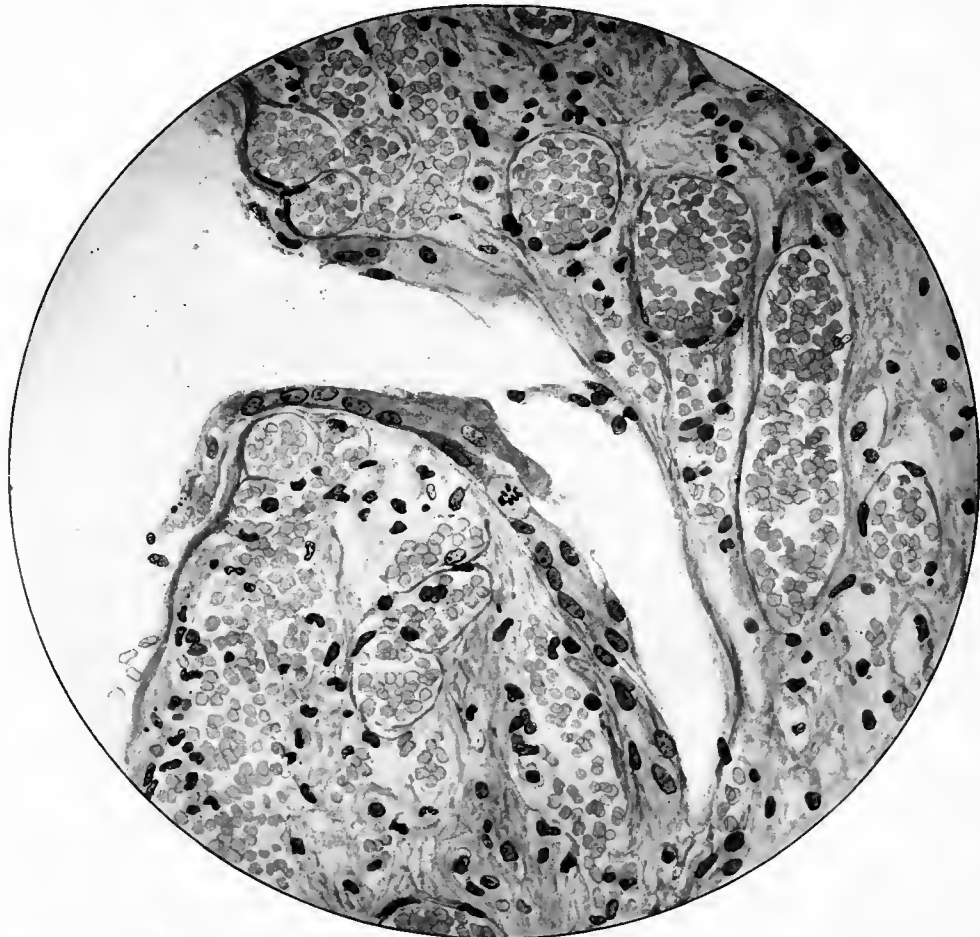


FIG. 15.—Case 61. Mustard-gas burn, 9 days' duration. Epithelial regeneration of trachea, proceeding from the mucous ducts

pronounced thickening of the wall, with narrowing of the lumen. As we have stated above, the granulation tissue might or might not be reinvested by epithelium according to whether the initial injury involved the epithelium of the mucous ducts or not.

In a few of the cases in which the mucous glands were injured it was possible to study a regeneration of these structures. The acinus was filled with a pink-staining, more or less hyaline, necrotic mass, embedded in which were nuclear particles. This represented the remains of the necrotic gland cells, and at the periphery the new secretory epithelium was seen pushing its way between the necrotic cells and the basement membrane of the gland.

LUNGS

The appearance of the lungs at autopsy presented a bewildering variety, and it is quite impossible to describe a composite picture which would distinguish the lungs of mustard-gas poisoning from those of the various types of pneumonia. Perhaps the most distinctive cases were the very early ones, in which the pulmonary lesions were largely confined to the bronchi and their immediate neighborhood. The lung was voluminous and did not collapse readily after removal. Occasionally the pleura was smooth, but in most cases there were patches of early fibrinous pleurisy. Darker sunken area of atelectasis

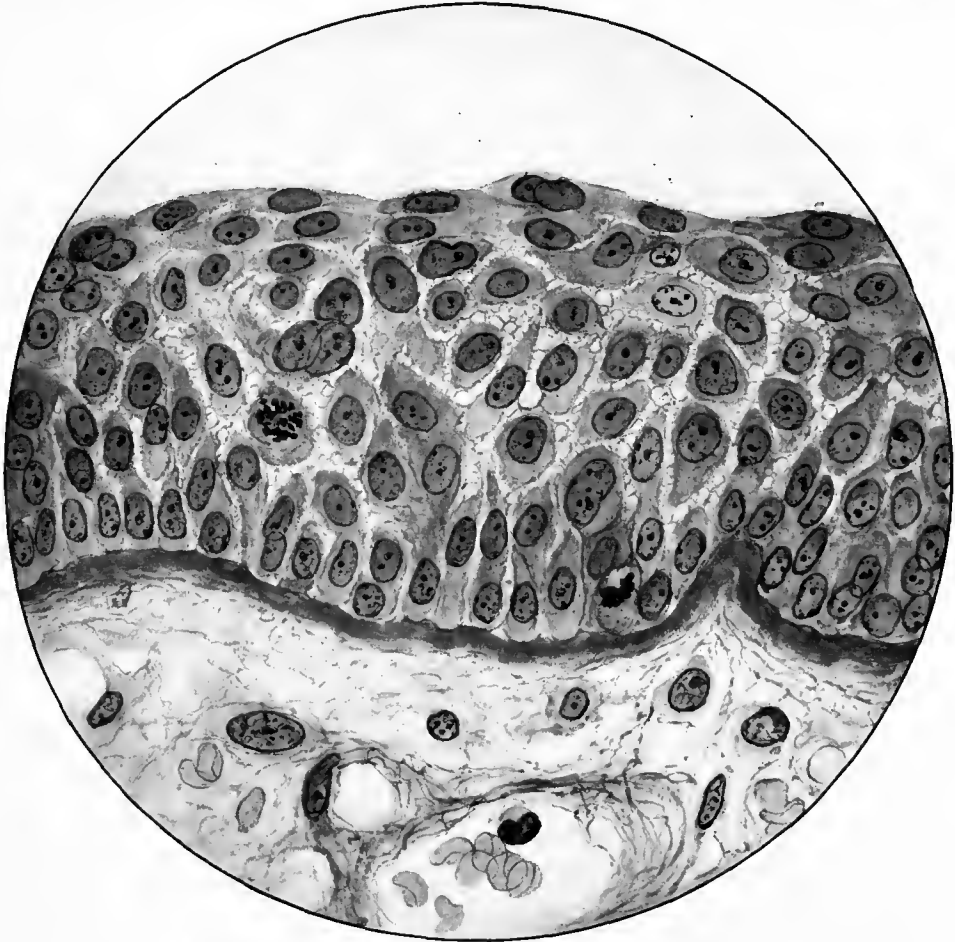


FIG. 16.—Case 41. Mustard-gas burn, 7 days' duration. Metaplasia of tracheal epithelium into squamous cell type. Numerous mitoses

associated with the occlusion of bronchi were visible on the surface. On section the most conspicuous features were the thickened bronchi filled with plugs of creamy fibrinopurulent exudate, or in the case of the smaller bronchi a droplet of creamy pus might exude. Each bronchus was surrounded by a dark red sunken areola 2 or 3 mm. in width. This last feature is regarded as particularly characteristic; the red peribronchial zone histologically was found to be composed of the adjacent alveoli, which were filled with red blood cells and more or less collapsed. Further outward from the bronchus the hemorrhage

gave place to a fibrinous exudate in which only a few desquamated alveolar cells and occasional leucocytes were included. (Pl. IX.) This peribronchial reaction did not appear to be due to a direct extension of the infection within the bronchus through the bronchial wall. It would seem that the hemorrhage was caused by the direct action of the toxic agent diffused through the wall of the bronchus. The collapse may perhaps be explained by the distension of the small bronchus with compression of the adjacent air spaces. Frequently, at least, the alveoli directly adjoining the bronchus appeared flattened.

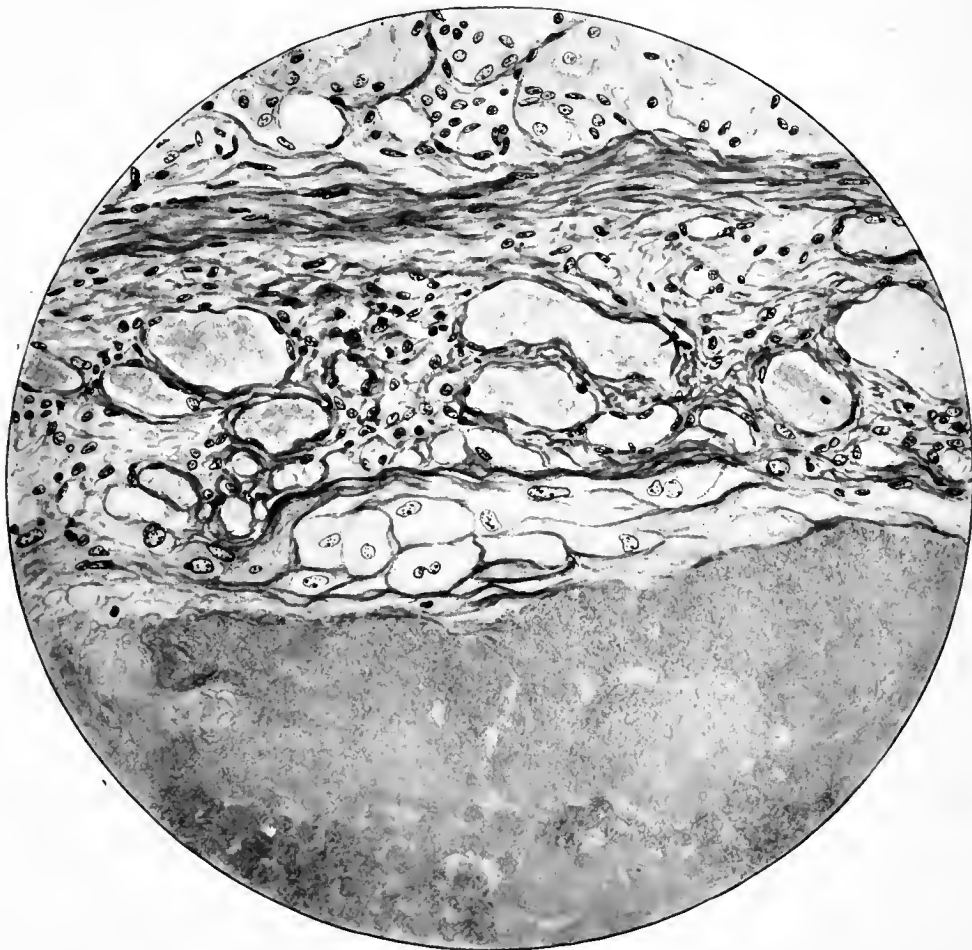


FIG. 17.—Case 24. Mustard-gas burn, 5 days' duration. Between the false membrane and the congested sub-epithelial tissue are interposed hydropic epithelial cells of the squamous type

Aside from these bronchial and peribronchial lesions the lung, on section, showed emphysema and darker areas of partial collapse. Edema was present to a greater or less degree in about two-thirds of the cases. It was never so extensive as in the lung of phosgene or other asphyxiating gas and was often patchy in its distribution, being much more marked in some portions of the lobe than in others. From the autopsy records, which naturally vary greatly in detail and accuracy, it appears that excessive edema was noted in only three cases occurring two and three days after gassing, and in one case in which

the period of survival was not established; moderate general edema was present in 28 cases and slight patchy edema in 43 cases. In 18 cases the absence of edema is specifically reported, and in 6 cases no record was made.

As with so many of the pulmonary lesions, it was difficult to decide whether this edema was the direct result of the action of the mustard gas upon the alveolar capillaries or whether it was due to secondary infection, to the failing circulation, or to other obscure factors. It is true that even in the early cases bacteria abounded in the bronchial and infundibular lesions. They were not usually present, however, in the edematous areas at a distance from the bronchi. This, and the fact that the most intense edema was recorded

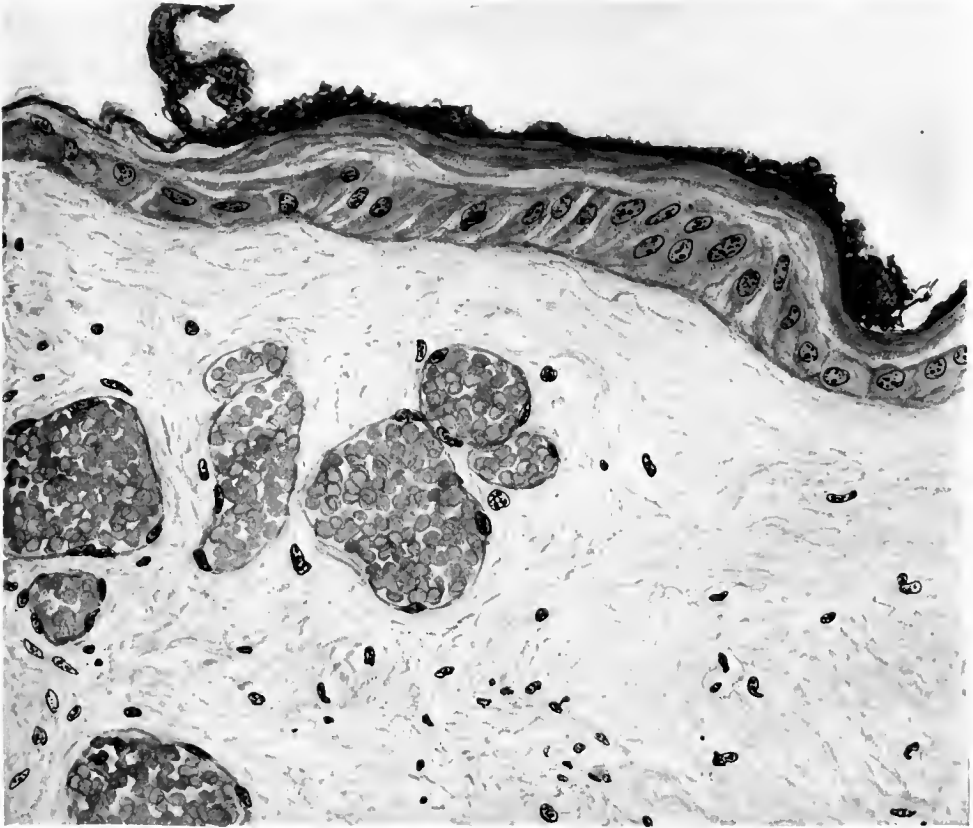


FIG. 18.—Case 89. Mustard-gas burn, 20 days' duration. Trachea. The regenerating epithelium is growing beneath the old swollen basement membrane, which covers the exposed surface

in relatively early cases, is perhaps an argument in favor of the direct edema-producing action of the mustard gas. Experimental observation also supports this view. It was possible in rabbits by intravenous injection to produce moderate pulmonary edema (Pappenheimer and Vance).⁶ Lynch, Smith, and Marshall made similar observations in dogs.⁷ In cases which died late the edema, when present, was in all probability secondary and not due to the initial chemical injury.

The great majority of the cases showed, in addition to the bronchial and peribronchial lesions, areas of focal pneumonia, sometimes small and nodular, often large and confluent. There was no constancy in the appear-

ance of these pneumonic patches, nor could one find sharply cut differences in the appearances in cases dying early after gassing and in those which survived for weeks or even months. A fresh bacterial infection might develop at any stage after the initial chemical injury, and it was not uncommon to find in the same lung recent and older organizing lesions.

During the height of the influenzal epidemic in October and November, 1918, many of the gas pneumonias exhibited the characteristic gross features which had come to be associated with the pulmonary lesions of influenza. The lungs were heavy and voluminous and often a dusky red, especially in the posterior portions. There were fresh pleural hemorrhages and more or less fine fibrinous pleurisy which became organized in the later cases. Only twice was the pleurisy suppurative in character; in one of these cases (Case

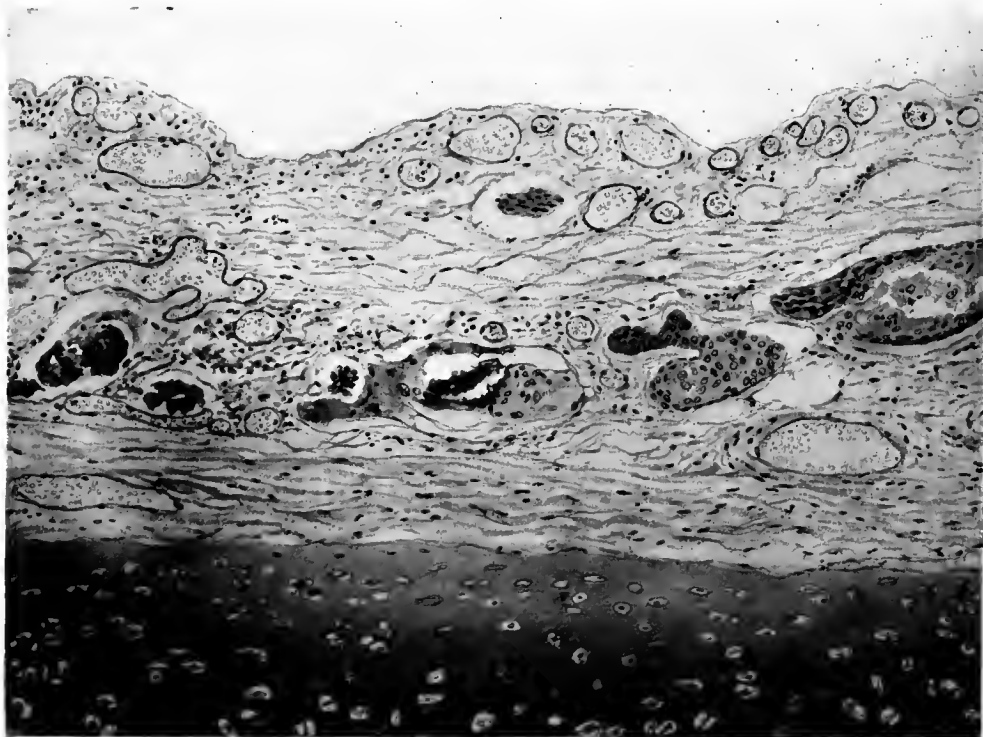


FIG. 19.—Case 86. Mustard-gas burn, 18 days' duration. Bronchus. Proliferation of epithelium of ducts of mucous glands

99), the empyema was due to the extension of a traumatic liver abscess; in the other (Case 25), which occurred in August, the pleurisy was not extensive, and the resemblance of the pulmonary lesions to those found in influenza were less striking than in many other cases.

On section these lungs showed, in addition to the characteristic membranous bronchitis and bronchiolitis and peribronchial areola, diffuse, often incomplete areas of consolidation associated with much hemorrhagic edema. (Fig. 20.) The greater portion of one or several lobes was frequently affected. In some of the later cases there are described also opaque grayish areas of necrosis and groups of small abscesses. Organization was not infrequently recognized in the gross by some of the more experienced pathologists and confirmed histologically. (Fig. 21.)

In describing the histological changes associated with this type of pneumonia attention is called again to the extraordinary resemblance of the finer changes to those observed in the primary influenzal cases. These lesions can not be ascribed wholly to the influenzal or postinfluenzal infection, in as much as they may be reproduced in animals by exposure to the gas alone, and have been present also in human cases dying at times when the epidemic was not active.

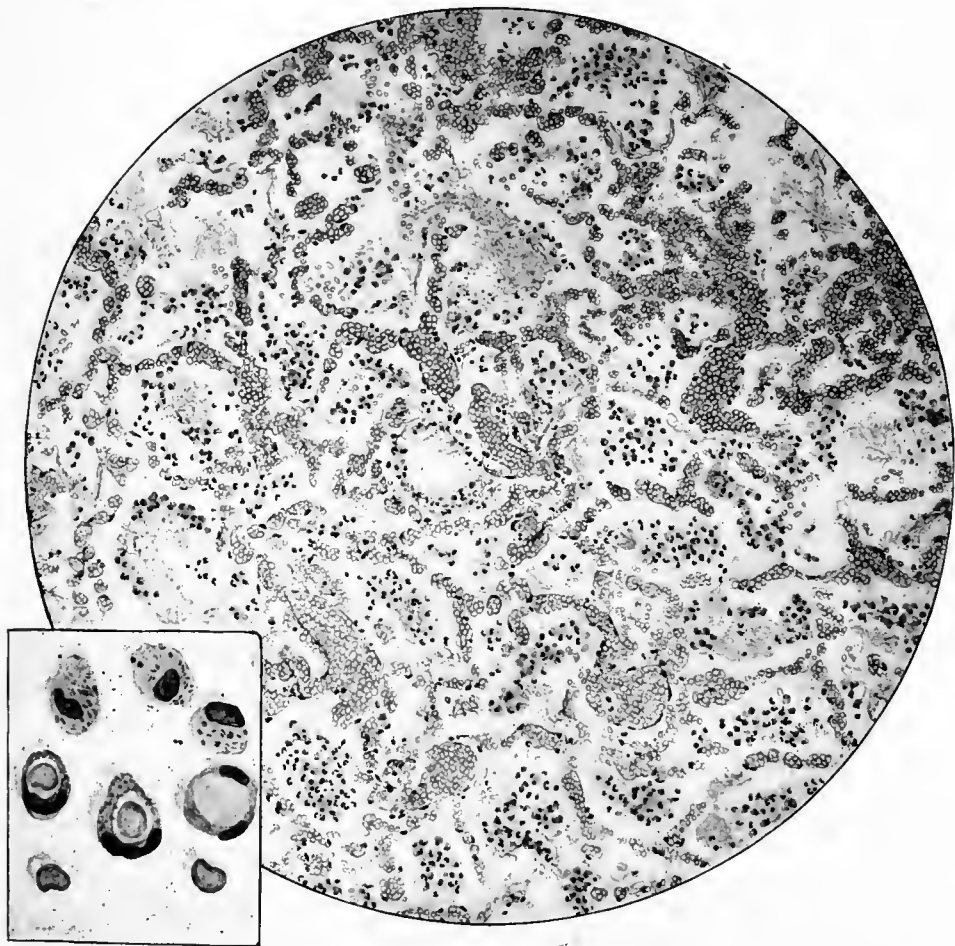


FIG. 20.—Case 28. Mustard-gas burn, 4-5 days' duration. Lung: Intense congestion, hemorrhagic edema, aplastic exudate. The leucocytes are filled with minute Gram-negative bacilli

Leaving aside the larger bronchi, which have been described and in which the membranous character of the necrosis is usually more extreme than in the primary influenzal cases, the terminal bronchioles were found usually with their ciliated epithelium more or less conserved. There was an acute suppurative inflammation, which was in nowise distinctive. The atria, however, were often widely dilated; they might or might not themselves contain exudate. (Fig. 22.) The wall was lined by a wavy hyaline band, which sometimes, but not regularly, gave a faint fibrin stain with the Gram-Weigert-safranine method. (Pl. VI.) It was a little difficult to be sure of the composition of this hyaline band. It

did not appear to be composed solely of the necrotic lining epithelial cells, although these probably took part in its formation. The continuity of the membrane with definite bands of fibrin in the walls of the atria or alveoli indicated that the fibrin was at least the chief constituent. Later, as it became more and more swollen and hyalinized, the specific staining was less readily obtained. In part it might have been due to the condensation of a highly albuminous material about the wall of the infundibulum.



FIG. 21.—Case 103. Mustard-gas burn, 58 days' duration. Lung: Organizing and interstitial pneumonia

The lesions found in the alveoli were manifold. The alveolar exudate in the vicinity of the bronchioles and atria was apt to be fairly cellular, containing, in addition to a variable number of red cells, leucocytes of various types, but predominantly polymorphonuclear. But there were large areas in which the exudate was characteristically poor in nucleated cells and was rather of the nature of a hemorrhagic edema. The fluid either contained a loose fibrin net or appeared merely as a homogeneous or fibrinous coagulum. There would be merely diapedesis of red cells or more profuse hemorrhages, leading to disruption and necrosis of the lung tissue and distinguishable from infarcts only by the absence of thrombi within the larger arteries. The alveolar capillaries

in these portions of the lung were tremendously distended, bulging into the alveolar spaces. (Pl. VI.) Sometimes it appeared as if the membrane upon which the endothelium rests was swollen and thickened. Fibrin thrombi were fairly often found within the capillary lumen, and in some cases were quite abundant. It was very common also to see coarse fibrin threads deposited in the septa between the capillary wall and the epithelium. Edema of the alveolar

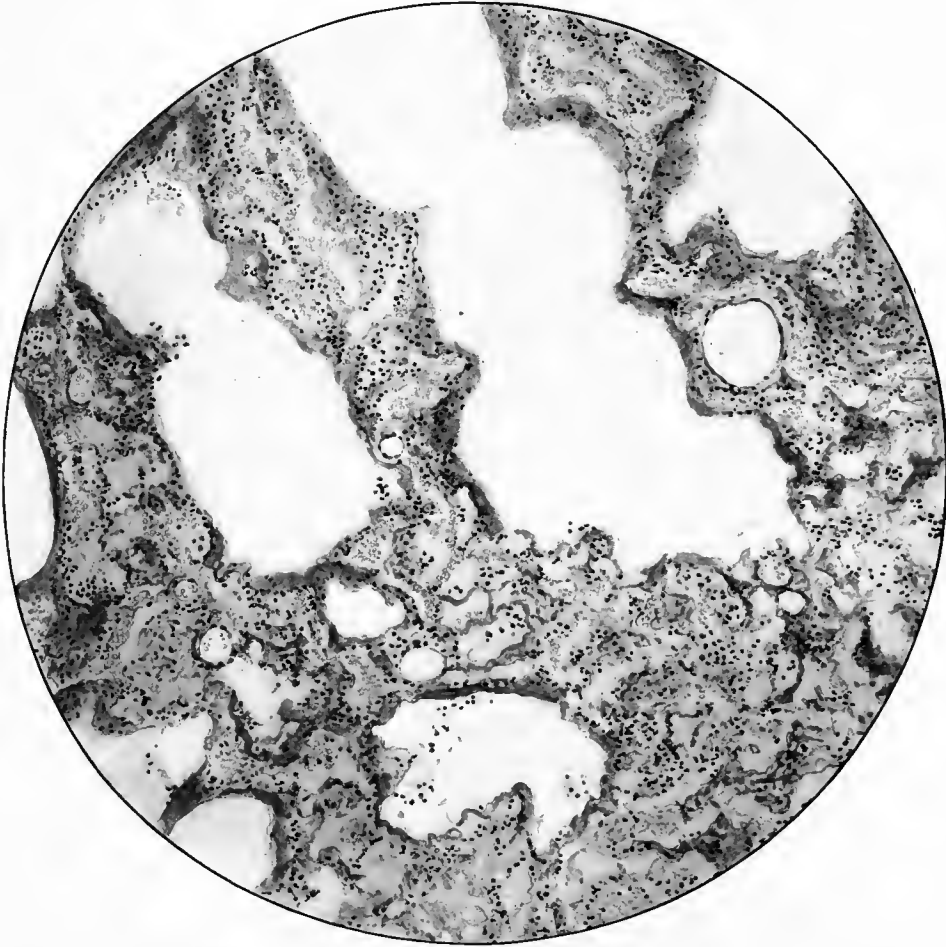


FIG. 22.—Case 81. Mustard-gas burn, 15 days' duration. Lung. Dilatation of alveoli, with hyaline necrosis

wall was often striking, and the still intact alveolar epithelium could be elevated at times as a continuous sheet of cells.

The alveolar epithelium itself in the early acute cases often appeared swollen and vacuolated, although it was only occasionally that degenerative changes could be recognized in the still adherent cells. There was always more or less exfoliation, the cast-off cells becoming rounded, taking up red cells, pigment granules, leucocytic nuclear fragments, losing their nuclear staining eventually, and becoming degenerated.

Necrosis of the capillary wall was observed repeatedly, with fragmentation of the endothelial nuclei and of the leucocytes, as recently described by Le Count in cases of primary influenzal pneumonia, and regarded by him as highly characteristic.⁸ (Fig. 23.)

Just as the bacteriological studies in influenzal pneumonia showed in the lung a varying flora, so the bacteriological data in the series of gas pneumonias studied failed to throw any light on the difference in anatomical types. Both

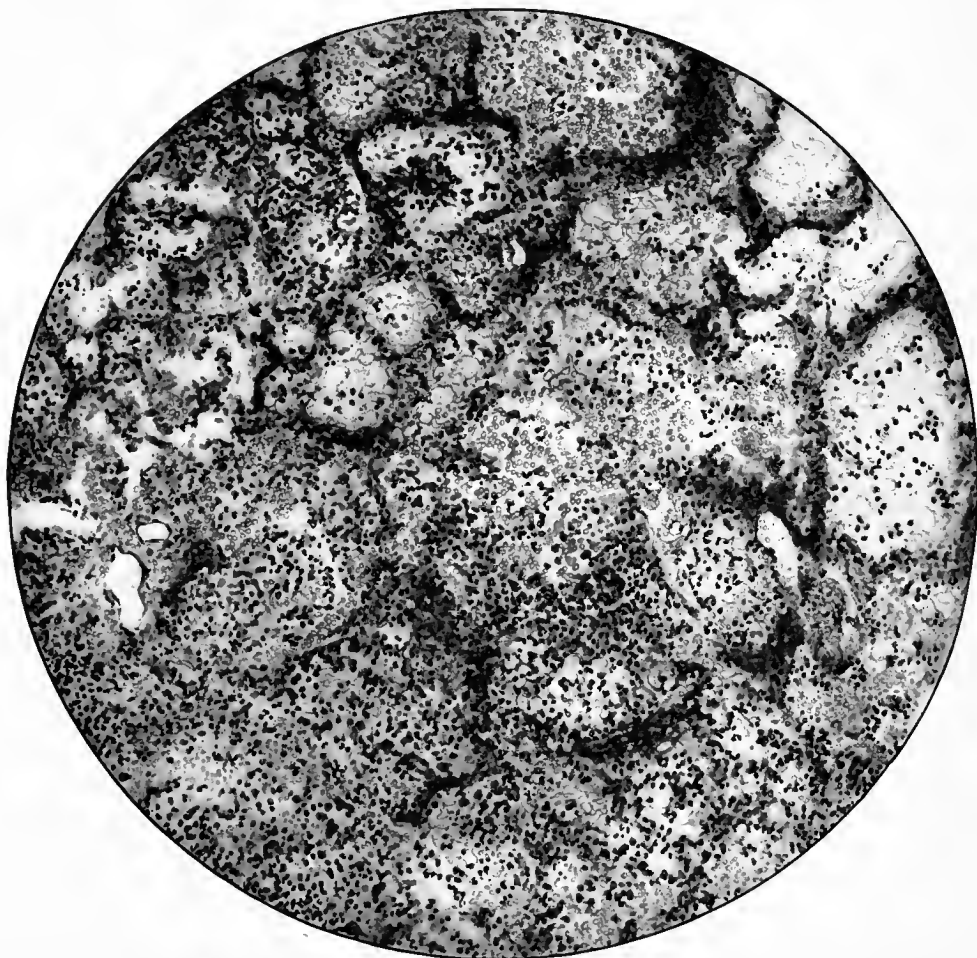


FIG. 23.—Case 22. Mustard-gas burn, 5 days' duration. Lung: Pneumonia, with necrosis of alveolar walls and nuclear fragmentation

culturally and in bacterial-stained sections a variety of forms was found. In a few cases, and these unfortunately were uncontrolled by cultures, the sections showed enormous numbers of minute Gram-negative rods as the predominating organism in the alveolar exudate. Many other cases, grossly and histologically similar, showed only Gram-positive cocci. So confusing were the findings that it seemed not worth while to attempt an analysis, particularly as no systematic study could be carried on.

REPARATIVE CHANGES

The regenerative changes in the trachea and larger bronchi have already been described. Although bacteria were always present, the destruction produced by the chemical irritant was of so gross a character that the rôle of the bacteria may well be regarded as altogether secondary, particularly as they rarely invaded the deeper tissues. The healing process also may be looked upon as a repair of the chemically injured tissue. But in the parenchyma of the lung,



FIG. 24.—Case 53. Mustard-gas burn (history of exposure also to green and blue cross shells), 8 days' duration. Lung, small bronchus, lined with dense granulation tissue; thickening of septa of adjacent alveoli, which contain plugs of dense fibrin undergoing early organization

where the original chemical injury was lost or overshadowed by the bacterial infection, it became quite impossible to say whether the reparative and organizing processes which were present in the later cases were in response to the chemical or the bacterial poison. But it was these late and permanent changes, however brought about, which were of the greatest practical interest, and it is necessary to describe them in some detail in order to form an approximate idea of the damage which may be expected to ensue upon the gassing.

The thickening of the walls of the small bronchi was an alteration which was quite evident in gross sections of the lung. The section showed the bronchial wall replaced by a vascular granulation tissue, with lymphoid and plasma cells predominating. Where the epithelial lining had failed to regenerate this granulation surface lay exposed, and it can not be doubted that the further contraction of this tissue would lead to narrowing or complete occlusion, with the formation of bronchiectases distal to the stenotic area. (Fig. 24.)

Bronchial stenosis, also might result, though apparently not so frequently as one might expect, from the organization of the exudate within the bron-

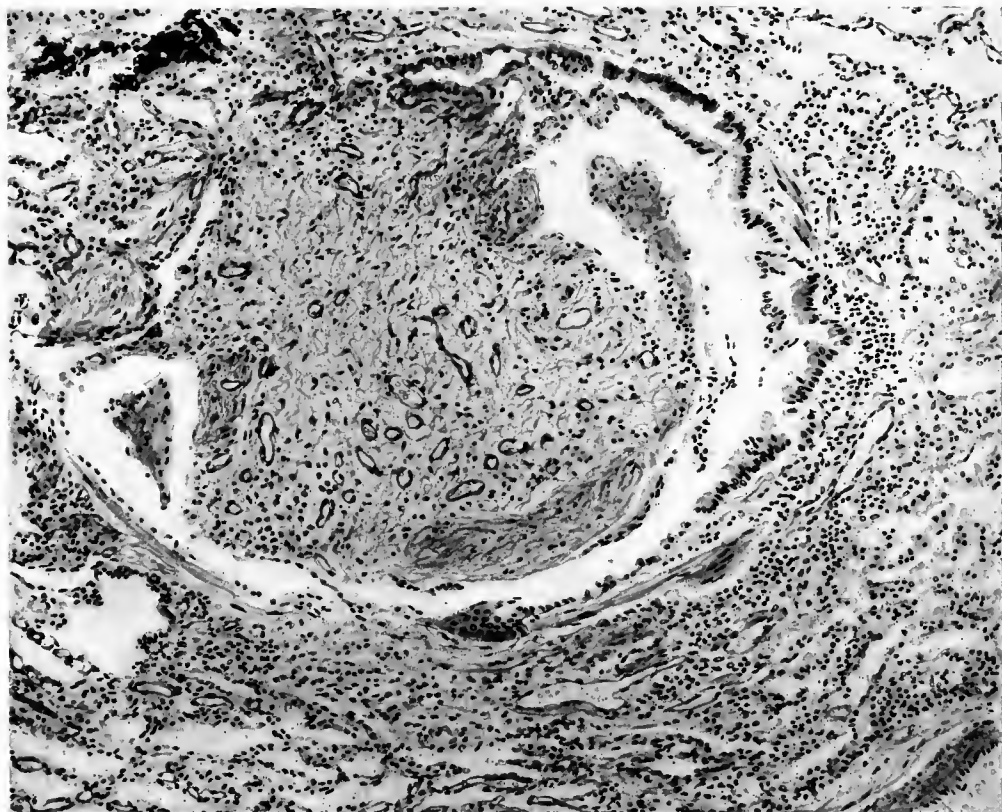


FIG. 25.—Case 100. Death, 51 days after exposure to mixed vesicant and suffocant gases. Section through dilated bronchiole, containing a vascular organized plug

chiole. This seemed to occur more often in the ductus alveolaris, where the organizing fibrinous plugs extended into the contiguous alveoli. (Fig. 25.)

The zone of atelectasis, hemorrhage, and fibrinous edema which so often encircled the medium-sized and smaller bronchi has been described. In this zone, where the fibrin offered support to the growing cells, active organization was regularly found in progress, even when the pneumonic process at a distance from the bronchi was in full blast. It was in this peribronchial zone also that there was found, as in the later stages of the primary influenzal pneumonias, a remarkable proliferation of the alveolar epithelium. The new cells, distinguished by their deeper staining, their cuboidal form, and often

by numerous kinetic figures, not only reinvested the cavities of the alveoli but grew over and even into the plugs of fibrinous exudate (Fig. 26), and in some instances formed solid, carcinoma-like nests of cells. The alveolar septa also were thickened by the growth of fibroblasts, the new-formed connective tissue being continuous with the granulation tissue about the small bronchi, and also with the new-formed fibrous tissue which invaded the edematous tissue about the arteries and interlobular septa.



FIG. 26.—Case 74. Mustard-gas burn, 12 days' duration. Lung. Proliferation of alveolar epithelium over a mass of fibrin and agglomerated red blood corpuscles

LESIONS IN OTHER ORGANS

The study of human cases afforded little evidence that mustard gas, through cutaneous application or by inhalation, could be absorbed and could produce systemic effects in other organs. In dogs exposed to high concentrations in the chamber, the hydrolysis product, dihydroxyethylsulphide, has been detected in the urine by reconvertng it into dichlorethylsulphide and obtaining a vesicant action upon the human skin (Lynch and Marshall).⁹ So far as is known no similar demonstration has been made in man.

Clinically there has been observed a group of cases with diffuse pigmentation, marked apathy and asthenia, low blood pressure, and often pronounced mental disturbances, symptoms which it is difficult to correlate with the obvious lesions of the skin and respiratory tract. Indeed, in some of these

cases, respiratory damage may be quite insignificant. Such cases certainly suggest a systemic intoxication of some sort, and Satre and Gaos,¹⁰ and other French clinicians have attributed the symptoms to an acute adrenal insufficiency. No anatomical evidence has been brought forward to incriminate the adrenals, and the observations are not sufficiently definite to justify any far-reaching conclusions. The lassitude and asthenia, and even the mental disturbances, in men freshly returned from combat, are perhaps more easily explained in other ways.

More direct proof of the absorption of dichlorethylsulphide are the changes in the bone marrow and in the circulating blood. Zunz,¹¹ Stewart,¹² and later Krumbhaar¹³ have shown that severely gassed cases, after an initial leucocytosis, may develop a marked leucopenia, and similar observations have been made by Muratet and Fauré-Fremiet in animals. Pappenheimer and Vance⁶ have also shown that intravenous injections of small doses in rabbits brought about a profound leucopenia, with destruction of the granulocytes in the bone marrow, an effect comparable in its specificity with that of benzol. This has been confirmed by Warthin and Weller.¹⁴ Krumbhaar and Krumbhaar have brought confirmation of their clinical evidence by a study of the bone marrow in human cases.¹⁵ It may be taken as proved, therefore, that when introduced into the body dichlorethylsulphide is a specific poison for the hematopoietic tissue, and there are both clinical and experimental reasons for believing that a similar effect follows the inhalation of massive doses.

LESIONS OF THE ALIMENTARY TRACT

Abdominal tenderness, anorexia, nausea, vomiting, and less frequently diarrhea were observed clinically in a large proportion of mustard-gas cases. The experiments of Warthin and Weller,¹² Lynch, Smith, and Marshall,⁸ Pappenheimer and Vance,⁶ and others, have shown that the intravenous or subcutaneous injection of dichlorethylsulphide in animals may be followed by a hemorrhagic enteritis. Norris¹⁶ refers the submucous hemorrhages of the stomach and duodenum to the swallowing of contaminated saliva, but the possibility of the elimination of the absorbed substance or its hydrolysis products through the alimentary tract has not been disproved. This possibility is suggested by the experimental facts cited above and on clinical grounds by Ramon, Petit, and Carrié.¹⁷

In the human protocols studied the alimentary tract was not examined in about half of the cases; in about 25 per cent of the cases the stomach and intestines are specifically stated to be normal; in the remainder there are noted injection or hyperemia, sometimes of the stomach, more commonly of the small intestine; hemorrhages in stomach, small or large intestines, erosions or small ulcers, in three cases in the stomach, once in the small intestine, once in the colon.

Too much weight should not be placed on these fragmentary references. The injection may be attributable to the general visceral stasis, which is the rule in the fatal cases. Hemorrhagic erosions of the stomach are so frequent a finding in any large series of autopsies that their occasional presence in these cases does not seem very significant. On the other hand, a more careful scrutiny might have shown a higher incidence of gastrointestinal lesions.

LESIONS OF THE LIVER

No changes were found apart from those common to all acute infections. Patients dying early have not shown degenerative changes which might be ascribed to a specific effect of the mustard gas.

LESIONS OF THE CIRCULATORY ORGANS

No anatomical alterations of the myocardium were found which might throw light on the late circulatory disturbances (effort syndrome) noted in a certain proportion of gassed individuals. Dilatation of the right side of the heart is not infrequently mentioned and may be regarded as secondary to the pulmonary lesions. It was not always evident at autopsy. Suppurative pericarditis as a secondary infection with hemolytic streptococci is recorded in one case. Nor was there found a typical or characteristic vascular lesion in the lung or elsewhere, which could not be of infective origin. That the frequent occurrence of rather marked pulmonary edema in the severe early cases implies an alteration in the permeability of the blood vessels may be assumed, but the cellular changes in the endothelium are not sufficiently definite to warrant description.

LESIONS OF THE KIDNEYS

Apart from incidental lesions, obviously antecedent to the gas poisoning, these organs showed only an intense venous and capillary congestion. In one case only were there hemorrhages into the capsular spaces and tubules. No alterations which would suggest a toxic effect upon the renal epithelium were noted. The intense congestion is probably sufficient to explain the diminished urinary output, albuminuria, presence of casts and red blood cells described by Hermann¹⁸ as typical urinary findings during life.

LESIONS OF THE CENTRAL NERVOUS SYSTEM

Unfortunately there were available no data upon possible finer alterations in the central nervous system. In very few cases was the brain examined, and in none of these were significant gross changes detected, nor was material for histological study preserved. Stewart¹² has described ring hemorrhages in the brain associated with swelling and degeneration of the endothelium, thrombosis, and slight leucocytic emigration.

LESIONS OF THE ORGANS OF INTERNAL SECRETION

No facts of value have been deduced from the incomplete study of the adrenal gland and other organs of internal secretion which have been occasionally included in the material studied.

DETAILED AUTOPSY PROTOCOLS OF 107 CASES, WITH MICROSCOPIC EXAMINATION OF TISSUES

The cases are arranged according to the period of survival after gassing. In the majority of the cases the date of gassing is accurately stated; in some it is inferred from the date of the first admission to field or evacuation hospital. Frequently additional data have been disclosed by the study of the reports of the gas officers of the Chemical Warfare Service, and the clinical records on file in the Office of the Surgeon General. Such information has been included

in the autopsy record. In a few instances, where the date of gassing is not given, it may be reasonably surmised from the fact that other members of the same company, battalion, or regiment were gassed about the same time and showed lesions similar in character. In only two cases was it not possible to obtain data roughly estimated from the character of the lesions.

While the effort has been made to present the records of the gross lesions as nearly as possible in the form and expressions used by the pathologist who performed the autopsy, it has been thought desirable to omit detailed descriptions of lesions irrelevant to the gassing and where necessary to alter the arrangement for the sake of uniformity. The reports will naturally be found to vary greatly in accuracy and completeness. Many of the autopsies were done under conditions where there was neither time nor facility for detailed observation and record. It seems hardly necessary to apologize for these defects.

CASE 1.—M. L., 64329, Pvt. Co. L, 192d Inf. Died, October 28, 1918, 2 p. m., Evacuation Hospital No. 7. Autopsy — hours after death, by Capt. James F. Coupal, M. C.

Clinical data.—Date of gassing not recorded. October 28, men of company were exposed to shell which had little odor, produced marked sneezing, with casualties five hours later. Severe dyspnea.

Anatomical diagnosis.—Not recorded.

Gross findings.—(The following note upon the lesions of the respiratory tract was made in the pathological laboratory, experimental gas field). The *pharynx*, *larynx*, and *esophagus* are normal. The *trachea* also shows no gross lesions. The primary and secondary *bronchi* show a reddened mucosa, covered with loose shreds of tenacious mucus. Their mucosa is intact. *Right lung*: Voluminous, weighs 735 grams. The pleura is smooth, mottled with darker patches which are slightly sunken. On section the lung is air containing in all lobes. There is a very moderate general edema, somewhat more marked in the anterior portion of the lung. *Left lung*: Weight, 705 grams; somewhat more voluminous than the right. The pleura is free from exudate. On section there is pretty marked general edema, with scattered patches of collapse. No pneumonic patches. The small bronchi are normal.

Microscopic examination.—*Trachea*: In some places the epithelium is definitely necrotic and replaced by a mucopurulent exudate, the membrana propria being interrupted in some of the eroded places. In other places the nuclei of the epithelial cells, which are reduced to a single row, are definitely pyknotic in comparison with the vesicular nuclei of the uninjured cells. The vessels of the submucosa are congested. *Lung*: The epithelium of the smaller bronchi is uninjured; the lumina contain a small amount of coagulum, desquamated cells and a few leucocytes. Many of the alveoli contain homogeneous, pink-staining material which is practically cell free. The septa are thickened and edematous. There is a stasis of leucocytes in the capillaries. No bacteria are found in sections stained with Gram-saffranine. *Myocardium*: There is distinct edema about the intermuscular vessels and of the connective tissue between the muscle bundles. *Liver, kidney, spleen, adrenal, and pancreas* show no significant lesions.

NOTE.—The lesions suggest exposure to a mixture of the suffocant and irritant types of gas, possibly phosgene and arsene compounds. There was definite necrosis of the bronchial epithelium such as one would not expect to find after phosgene alone. The absence of bacterial growth and secondary pneumonic lesions may be taken as evidence of early death in this case, probably within 24 hours.

CASE 2.—A. D., 1429216, Pvt. Hdqrs. Co., 39th Inf. Died, October 11, 1918, 4.45 a. m., Evacuation Hospital No. 6. Autopsy, five hours after death, by Capt. James F. Coupal, M. C.

Clinical data.—Gassed October 10, near Verdun, blue cross and green cross shells. Clinical diagnosis of phosgene poisoning.

Anatomical diagnosis.—Edema and congestion of lungs; emphysema; bronchopneumonia.

External appearance.—Marked post-mortem lividity. No burns of skin. Quantities of frothy fluid exude from mouth.

Gross findings.—*Pleural cavities:* Very slight retraction of lungs after removal of sternum. Each cavity contains about 60 c. c. of straw-colored fluid. *Lungs:* Voluminous and extremely mottled, dark red areas of congestion alternating with pink areas of emphysema. On section the left lung especially shows numerous miliary areas, apparently connected with the finest bronchi. On examination with a hand lens these are found to be composed of aerated alveoli surrounded by dark red edematous and congested lung tissue. This appearance is less pronounced in the right lung. The parenchyma in general shows intense congestion but relatively little edema. *Neck organs:* Tonsils and lymphoid tissue at the base of the tongue enlarged. The mucosa is smooth, velvety, much congested, but there is no ulceration or exudate. The *smaller bronchi* appear normal. *Heart:* Cavities of right side extremely dilated. Remaining organs show no distinctive changes. *Gastrointestinal tract:* Not recorded.

Microscopic examination.—*Trachea and bronchi* of larger caliber: Ciliated epithelium is lost. The superficial cells show pycnosis of their nuclei and a homogenization of the cytoplasm. In occasional cells are found hydropic vacuoles with crescentic compression of the nucleus. The membrana propria is thick and swollen. The blood vessels of the submucosa are congested, but there is no hemorrhage and little or no inflammatory reaction. (See fig. 3.) *Lungs:* The small bronchi show a normal epithelium which is often desquamated or elevated in strips from the underlying basement membrane by a collection of edematous fluid. The infundibula are dilated; they have no epithelial lining. The surrounding alveoli show marked changes consisting of edema, hemorrhage, desquamation of epithelium, and the presence of numerous pigment cells. There are excessive numbers of polynuclears in the capillaries, the nuclei of which, especially in the neighborhood of the infundibula, show striking distortion and fragmentation. Elsewhere there is patchy edema, the coagulum being homogeneous and containing little fibrin. Gram-positive cocci are found both in the bronchi and in the alveolar coagulum. *Liver, spleen, and adrenals:* No significant changes.

NOTE.—In spite of the clinical history of phosgene, and the gross appearance of the lung, the lesions suggested the admixture of an irritant gas, possibly an arsene compound, acting especially upon the infundibula and the adjoining lung tissue. There was no extensive bacterial infection of the lung, masses of bacteria being found only in the small bronchi.

CASE 3.—C. G., French soldier. Died, October 8, 1918, at S. a. m., Gas Hospital, Julvé-court. Autopsy, six hours after death, by Capt. James F. Coupal, M. C.

Clinical data.—Gassed with phosgene on October 7. Died suddenly after sitting up, without great preceding dyspnea.

Anatomical diagnosis.—Massive pulmonary edema; dilatation of right heart; acute tracheitis.

External appearance.—The body shows marked lividity.

Gross findings.—*Pleural cavities:* Each contains about 300 c. c. of blood-stained fluid. *Respiratory organs:* (Note dictated upon receipt of specimens at the pathological laboratory, experimental gas field.) *Larynx:* Shows no edema. *Trachea:* Is discolored dark purplish-red. *Bronchi:* Contain frothy fluid and their mucosa is stained with blood. *Right lung:* Extremely large and dark purplish in color; the surface is smooth, the lobular markings being entirely obliterated. On section the lung is dark, firm, and rubbery, but showing no evident pneumonic consolidation; there is most intense edema, bloody fluid dripping from the cut section. The smaller bronchi do not contain purulent exudate. *Left lung:* Differs from the right in the appearance of the lower lobe, which, in its lower portion, is somewhat grayish, dryer, and more granular than elsewhere, suggesting early pneumonic consolidation. *Gastrointestinal tract* and remaining abdominal viscera normal save for congestion. *Heart:* Right side markedly dilated, left ventricle in extreme contraction.

Microscopic examination.—*Trachea:* There are definite lesions in certain areas. Where the epithelium is entirely defective the nuclei of the underlying connective tissue cells and lymphoid cells show marked karyorrhexis, and there is superficial necrosis, with groups of Gram-positive cocci in the necrotic tissue and in the blood vessels. There is also super-

ficial hemorrhage. Lesser injury to the epithelium is indicated by vacuolization of individual cells, or hyaline, pink staining of their cytoplasm. Where the epithelium is intact and composed of several layers, there is loss of cilia; but efforts at repair are suggested by the presence of numerous mitoses. *Lungs*: Sections of various blocks show similar picture. The alveoli are widely distended. The alveolar capillaries are wide and crowded with decolorized red blood cells. In the larger vessels the red cells are better preserved. In some of the septa it is possible to make out extravasation of cells between the capillary and the somewhat swollen basement membrane upon which the alveolar cells should rest. There is slight diapedesis into the alveolar spaces. The capillaries contain moderate numbers of mononuclear and polymorphonuclear leucocytes, some in process of emigration. A few alveoli contain dense collections of pyenotic leucocytes and much granular coagulum. The alveolar epithelium is not distinguishable. There is no fibrin. In some sections the edema is more evident, as shown by the abundant pink-staining coagulum. Sections stained for bacteria show enormous numbers of Gram-positive cocci in chains, pairs, and groups. They are found in the connective tissue about the blood vessels, in the septa outside the capillaries, and within the polymorphonuclear leucocytes of the alveolar exudate. No other types of bacteria are present. *Liver, spleen, kidney, and adrenals* show no significant changes.

NOTE.—A case of poisoning by suffocative gas, probably phosgene. There appears to have been complete death of alveolar epithelium, with massive invasion of bacteria (streptococci?) and hemolysis. The bacterial growth was probably not postmortal, since the autopsy was performed within six hours after death. There was very little inflammatory reaction.

CASE 4.—H. R., 76213, Pvt. Co. B, 18th Inf. Died, August 8, 1918, Gas Hospital No. 4. Autopsy, 11 hours after death, by Lieut. Russell W. Wilder, M. C.

Clinical data.—October 7, exposed to bombardment of phosgene and mustard-gas shells (77.105.150 mm.). Clinical diagnosis: Phosgene poisoning.

Anatomical diagnosis.—Diffuse generalized edema of lungs; anthracosis; hydrothorax, bilateral; dilatation of the heart; hyperemia of laryngeal and tracheal mucosa; cloudy swelling of liver and kidneys.

External appearance.—Marked cyanosis of ears, lips, and fingers, and extensive lividity of all dependent parts. Frothy serosanguineous discharge exudes from the mouth and nostrils. The skin shows no burns, scars, wounds, or abrasions. The eyes are clear, the lids edematous.

Gross findings.—*Lymph glands* are small. *Lungs*: Do not collapse and completely fill the pleural cavities. They show the imprint of the ribs. Right pleural sac contains 200 c. c. of serosanguineous watery exudate; the pleura is everywhere smooth and glistening. The left is like the right. The lungs are heavy and boggy, and when cut show an extremely wet surface. There is much anthracotic pigmentation. Several accumulations of air appear subpleurally over the surface, and the lung markings are emphysematous. *Neck organs*: There is moderate hyperemia of the mucosa of the pharynx and trachea, but no edema, tumefaction, exudation, or ulceration. The trachea shows slight hyperemia but no further change. It is filled with frothy serosanguineous fluid, which exudes in quantity when the lungs are pressed. *Heart*: Enormously dilated, especially the right auricle and ventricle, which are three times their normal size and filled with dark clotted blood. *Liver*: Intense congestion and cloudy swelling. *Spleen*: Four times normal size and very firm. *Kidneys*: Congestion and cloudy swelling. *Gastrointestinal tract*: Not recorded.

Microscopic examination.—*Trachea*: Lined with a single row of nonciliated cells, which are in some places completely exfoliated. The superficial cells have been desquamated. There is no edema or leucocytic infiltration of the submucosa, but the membrana propria unquestionably is thicker than normal. *Lungs*: Sections show advanced post-mortem changes, and finer details can not be made out. There are scattered patchy areas of edema. In some of the alveoli are many polymorphonuclear leucocytes, in the majority, the cellular elements are scanty and composed chiefly of desquamated epithelial cells containing pigment, red blood cells, and occasional leucocytes. Gram-positive bacteria are fairly numerous. There is little fibrin. Interspersed amongst the edematous and pneumonic areas are patches of collapse and emphysema.

NOTE.—The gross findings are very typical of acute poisoning by phosgene or similar suffocant gas, and confirm the clinical diagnosis. The histological material is of little value for finer study.

CASE 5.—H. E. McH., 3173285, Pvt. Co. H, 16th Inf. Died, October 4, 1918, Evacuation Hospital No. 6. Autopsy, October 5, 1918, — hours after death, by Capt. James F. Coupal, M. C.

Clinical data.—Mustard-gas burns and inhalation. Died while being evacuated.

Anatomical diagnosis.—Extensive superficial burns. Diphtheritic tracheobronchitis. Bronchopneumonia (bilateral).

External appearance.—Cloudiness of cornea and conjunctivæ. Burns of face, hands, elbows, and back.

Gross findings.—*Pleural cavities:* Left contains 40 c. c. of cloudy fluid. Right, negative. *Heart:* Right ventricle and auricle dilated. Otherwise normal. *Lungs:* Do not retract on opening chest cavity. *Left:* Early pleurisy over posterior portion. Lung on section is purple and yields quantity of blood and frothy mucus. Both lungs show areas of congestion and beginning consolidation scattered throughout. *Trachea:* Contains a false membrane which hangs to the wall and is surrounded by a quantity of thick mucus. *Gastrointestinal tract:* Negative except for injection of small intestine. The remaining organs are normal.

Microscopic examination.—*Trachea* and *larger bronchi* are covered by thick pseudomembrane which is made up of a fibrinous network in the interstices, in which are numerous polymorphonuclear leucocytes. The mucous glands show epithelial degeneration, possibly in part post mortem. The cartilages are normal. *Lungs:* Marked injection of all blood vessels, including the alveolar capillaries. In some areas the alveoli contain an eosinophilic granular debris, and the exudate is frankly inflammatory, the alveoli being filled with plugs of fibrin and leucocytes or merely leucocytes. Some alveoli contain large epithelioid cells which are filled with brown pigment. The smaller bronchi are acutely inflamed. Some contain a fine, purulent pseudomembrane, or a covering of leucocytes. Around one bronchus is an especially marked zone of congestion, and even an infiltration of red blood cells into the adjacent alveoli. *Liver:* Shows extensive fat infiltration. The remaining organs are free from significant changes.

NOTE.—The case is a typical one of early mustard-gas poisoning, with very extensive tracheobronchitis and early bronchopneumonia, dying on the second day after exposure.

CASE 6.—W. D. F., 3173197, Pvt., Co. H, 16th Inf. Died, October 4, 1918, at 2.20 p. m., Gas Hospital, Julvécourt. Autopsy, October 4, three and one half hours after death, by Capt. James F. Coupal, M. C.

Clinical data.—Mustard gas on the morning of October 2, 1918.

Anatomical diagnosis.—Multiple burns of skin; necrosis of tracheal and bronchial mucosa; bronchopneumonia; pulmonary edema.

External appearance.—Burns of face, neck, left hand, elbows, buttocks, and scrotum.

Gross findings.—*Pleural cavities:* The right pleural cavity contains 50 c. c. of clear fluid. Left, negative. *Lungs:* Contract only slightly. *Pericardium:* Contains 40 c. c. of clear fluid. The right heart is markedly dilated; left, in contraction. Otherwise negative. *Lungs:* The parenchyma of both lungs is congested. In the right middle lobe near the anterior border are patchy areas of atelectasis and bronchopneumonia in a stage of gray hepatization. Also a few areas of consolidation in right lower lobe. In the posterior portion of the left lung in both lobes are several deeply congested dark-red areas, somewhat resembling infarcts. The unconsolidated portion of the lung yields a quantity of frothy fluid. Mucosa of trachea appears necrotic and when stripped leaves an injected wall. The smaller bronchi contain a rather thin purulent exudate.

Microscopic examination.—*Trachea:* The epithelium is lost save for a single row of cuboidal cells here and there, and the epithelium of the ducts of the mucous glands which tends to creep over the adjacent tissue. The submucosa is slightly edematous. The nuclei of the connective tissue cells and of the wandering cells (chiefly polymorphonuclear leucocytes) which infiltrate the tissue in moderate numbers, are distorted and caryorrhectic. The blood vessels are rather wide and contain unaltered cells. Mucous glands normal. *Lungs:* Areas

of lobular pneumonia with foci of necrosis, patchy alveolar edema, and an excess of leucocytes in capillaries. (Fig. 27.) There is marked congestion and hemorrhage. The alveolar epithelium appears to be largely desquamated. It can rarely be made out distinctly. Bacteria are quite numerous, predominantly Gram-positive diplococci in the alveolar exudate and walls. Long chained streptococci and Gram-negative cocci and bacilli are also found, especially in bronchi. Bacteria are particularly numerous in the areas of necrosis. Fibrin is not abundant in the exudate, but is often present in the walls of the alveoli, apparently outside the capillary walls. A very interesting feature of the section is that many of the alveoli are lined with a hyaline, wavy, refractile band, which in Gram-Weigert-safranine preparation stains bluish but has not the definiteness of fibrin. (Sec Pl. VI) No alveolar cells overlie this membrane. It is difficult to make out whether it is swollen fibrinous

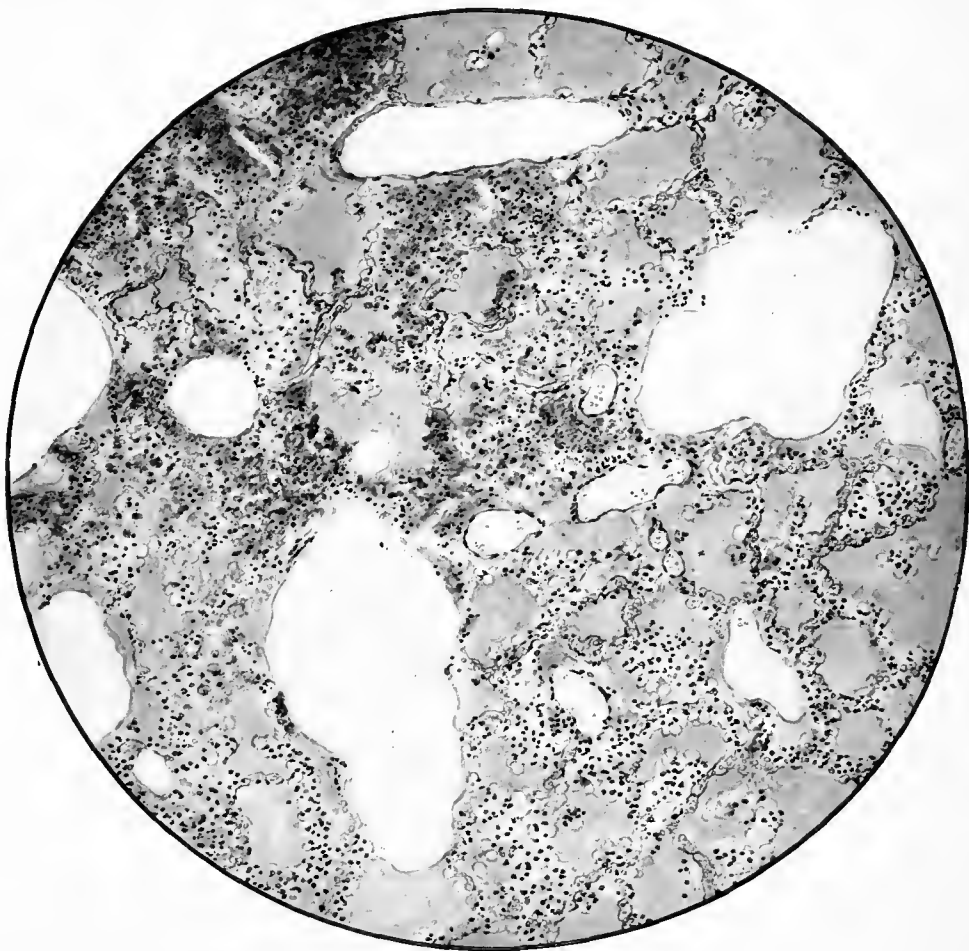


FIG. 27.—Case 6. Mustard-gas burn, 2 days' duration. Lung showing patchy alveolar edema, stasis of leucocytes in capillaries, beginning lobular pneumonia, with areas of necrosis, dilatation of atria

exudate, the membrana propria of the alveolar epithelium, or the hyaline necrotic alveolar epithelium itself. In favorable places it is seen to be raised up from the alveolar capillary, polymorphonuclear leucocytes and red blood cells being found beneath it, as well as in the alveolar space. *Liver:* Normal.

NOTE.—Definite history of mustard-gas poisoning, patient dying on second day. Typical mustard-gas burns. Lesions of the upper respiratory passages were rather superficial. Pneumonia was of the influenzal type, with hemorrhagic edema and hyaline necrosis of the alveolar and bronchial walls. Bacterial infection was already established.

CASE 7.—V. O., 134765, Pvt., Battery B, 2d Mass. F. A. Died, October 13, 1918, Julvé-court Gas Hospital. Autopsy, October 13, at 2 p. m., by Capt. James F. Coupal, M. C.

Clinical data.—Gassed with mustard gas 48 hours before death. Marked dyspnea.

Anatomical diagnosis.—Multiple superficial burns of skin; acute ulcerative tracheitis; purulent bronchitis; bronchopneumonia; acute fibrinous pleurisy; acute parenchymatous nephritis; mustard gas poisoning.

External appearance.—Marked post-mortem lividity. Burns of conjunctivæ, corneæ, axillæ, elbows, and scrotum.

Gross findings.—*Heart:* Markedly enlarged, right heart dilated. Muscle pale. *Lungs:* Retract only slightly upon opening the pleural cavity. Few fresh fibrinous adhesions over major portion of both lungs. Both lungs markedly edematous, especially in the posterior part, with the alternating areas of consolidation, congestion, and emphysema, the last especially along the anterior margins. Quantities of dark-red blood and frothy mucus can be scraped from the surface. *Neck organs:* Base of tongue and larynx are markedly congested. Mucosa of trachea is necrotic. Lumen filled with purulent exudate. Same condition extends throughout bronchial tree. *Gastrointestinal tract:* Not recorded. *Liver, spleen, and kidneys* show marked congestion.

Microscopic examination.—*Trachea:* Epithelium is desquamated over surface of mucosa except for a few flat epithelial cells in one area. Epithelium of gland ducts, however, though damaged, is more or less intact. A little fibrinous pseudomembrane is present. This is infiltrated with polymorphonuclear leucocytes and attached to the submucous layer. The latter is congested, edematous, and infiltrated with polymorphonuclear leucocytes, especially the superficial zone. The nuclei are caryorrhectic. The mucous glands and the deeper layers are not involved to the same extent. A few capillary thrombi are present. *Lungs:* The sections show no large bronchi, but some branches show desquamated epithelium and contain detritus and leucocytes. The alveolar walls are everywhere congested. Capillaries are distended with blood and contain leucocytes in excess. In one section the alveoli contain granular débris in which are large epithelioid cells with relatively small spherical nucleus, often containing brown pigment in the cytoplasm, and are accompanied by mononuclear and polymorphonuclear leucocytes and little fibrin. There is also more definite bronchopneumonia. Gram-stained sections show great numbers of streptococci. *Skin:* Entire layer of stratified squamous epithelium has been raised from the subcutaneous surface except for small areas near the mouths of the hair follicles. This portion of the epithelium is thin and the cells distorted and deeply pigmented. The subepithelial layer contains inflammatory cells of various types, some of which show abundant chestnut-brown pigment. Capillaries are congested, and elsewhere vessels are surrounded by small round cells. Sebaceous glands and hair follicles are not much affected. Sweat glands are normal. *Liver:* Congested and atrophied with central fat infiltration. *Spleen and kidneys* are negative.

NOTE.—Mustard-gas poisoning, death after 48 hours, with skin burns. There was necrosis of the epithelium of the trachea and bronchi, with very little membrane formation. There was early lobular pneumonia, probably streptococcal.

CASE 8.—O. K. McD., 45325. Pvt., Co. L, 18th Inf. Died, October 5, 1918. Autopsy at Evacuation Hospital No. 7, on following day, by Capt. James F. Coupal, M. C.

Clinical data.—Gassed October 3, mustard-gas shell. No autopsy protocol.

Gross findings.—(The following note of lesions of the respiratory tract was made at the pathological laboratory of the experimental gas field.) The *epiglottis* and *larynx* show no edema. Mucous membrane of trachea and large bronchi is reddened. There is no evident necrosis, exudate, or false membrane. The lymph nodes at the bifurcation are calcareous, showing obsolete tuberculosis. *Left lung:* Over the upper lobe are organized apical adhesions. There is a small area of collapse near the anterior border. On section there is moderate general edema and congestion. At the base of the lower lobe there is a circumscribed dark red area of consolidation about 3 cm. in diameter. The lower lobe is somewhat more edematous, congested posteriorly, with small patches of collapse scattered throughout the lung. Near the base is an area of consolidation somewhat grayer than that in the upper lobe. *Right lung:* The upper lobe shows edema and congestion, with a few small areas of consolidation near the hilus. The middle lobe is congested posteriorly, and anteriorly there are areas of atelectasis. There are a few small pneumonic areas in the base of the lower lobe. Some of the bronchi are found filled with thick mucopurulent exudate and surrounded by a narrow zone of collapse.

Microscopic examination.—*Lung and trachea:* There is a pseudomembrane present and the epithelium is destroyed. The submucous layers are edematous and infiltrated with polymorphonuclear leucocytes. The smaller bronchi are similarly inflamed but there is no pseudomembrane. The epithelium is intact in some bronchioles but the lumina contain masses of pus cells. The lung parenchyma is edematous and congested. The alveolar capillaries are infiltrated with leucocytes, some of which have wandered out into the alveolar spaces. In the alveoli are present also red blood cells, pigmented epithelial cells, and occasionally a small amount of fibrin. There is hyaline fibrinous material deposited in places in the alveolar septa. *Skin:* The normal epithelial covering is destroyed except around the mouths of two hair follicles. Even here the basal cells are in the process of vacuolization, elongation, and destruction, while the overlying layers are flattening out and disappearing. On the surface there is noncellular cornified membrane underneath which is a collection of red blood cells, leucocytes, and detritus, while the base of this blister is formed by the subcutaneous tissue, infiltrated by polymorphonuclear leucocytes, and is edematous. *Liver, spleen, and kidneys* show no significant lesions.

NOTE.—Mustard-gas poisoning, with typical skin lesions, death occurring on the second day after exposure. The respiratory lesions are rather indefinite and the histological description does not correspond with the gross findings, particularly as regards the presence of a membranous necrosis in the bronchi.

CASE 9.—C. H. W., 101135, Pvt., R. A. F., 3 Kite Balloon Section. Died, October 23, 1918, at 7.05 a. m., at Base Hospital No. 2. Autopsy, two hours after death, by Capt. B. F. Weems, M. C.

Clinical data.—October 21, 1918. Admitted to No. 47 Casualty Clearing Station, with gas-shell wound of right leg and groin. Gassed. October 22, admitted to Base Hospital No. 2. Face badly burned; eyelids edematous; slight cyanosis and dyspnea; rattle of moisture in trachea and bronchi; pulse 120. *Chest:* Good resonance, bronchial and tracheal râles. *Heart:* Cardiac dullness within normal limits. *Abdomen:* Superficial wound in epigastric region. Abdomen soft. Penetrating wound of left groin. Through-and-through wound of right thigh. October 23. No change in condition. Died suddenly at 7.05 a. m.

Anatomical diagnosis.—Extensive first and second degree burns of skin; acute conjunctivitis; membrano-ulcerative pharyngitis and tracheitis; laryngitis; membranous bronchitis; lobular pneumonia; congestion and edema of lungs; interstitial emphysema of lungs; acute fibrinous pleurisy, left; chronic fibrous pleurisy over right upper lobe; congestion of abdominal viscera; gas-shell wounds of both thighs.

External appearance.—Extensive burns over the trunk and extremities and large, pale-yellow blebs upon the anterior surface of both thighs, about the left knee, upon both forearms, and upon the neck and face. Besides these clear bullæ, there are large areas of a peculiar dusky, pinkish-purple color, in most cases adjacent to the bullæ and having approximately the same distribution. The face is swollen and covered over the bearded portions by scabby exudate; the skin about both eyes is swollen and discolored; there is purulent conjunctivitis. A mucopurulent exudate issues from the nostrils. There is extensive gingivitis. Skin over scrotum and penis edematous and in part blistered. *Wounds:* There is a through-and-through wound of right thigh, external to femur; wound of entrance just beneath anterior superior spine.

Gross findings.—*Lungs:* Marked inflation, anterior edges overlapping to level of third rib. Fibrous adhesions over right apex, no fluid in pleural cavities. Right, voluminous, color gray, becoming pink near posterior portion. The organ crepitates throughout. There are a few small slightly nodular areas in lower lobe. On section through upper lobe some small slightly sunken areas of a deep-red color are revealed, and a few small, rather cheesy plugs in the small bronchi. The lower lobe presents the same picture, except that there are a few patches of incomplete consolidation in lower portion and somewhat more congestion. Left, likewise voluminous, rather heavier than right, pleural surface shows a very slight fibrinous exudate, especially over anterior part of upper and lower lobes. There is some interstitial emphysema, most marked upon the anterior flap of upper lobe. The organ is closely nodular. There are lobular elevations over the anterior and inferior portions of upper lobe as well as lower. Upon section, surface is very moist, exuding bloody serum. There is patchy and extensive but incomplete consolidation. There are sunken brownish-red areas about the smaller bronchi. The bronchi themselves stand out sharply from the surrounding

tissue and appear almost occluded by fatty-looking plugs of exudate. Upon dissecting the larger bronchi these are found to contain large fatty looking casts coextensive with the tracheal membrane and extending downwards into the smallest bronchial tubes. *Organs of neck:* Tongue and regions about tonsils appear normal. The uvula is edematous and mucous membrane slightly macerated. The posterior pharyngeal wall is inflamed, with a slight fibrinous exudate. The laryngeal surface of the epiglottis and the epiglottic folds are edematous, deeply injected, and covered by a somewhat patchy grayish-yellow membrane. There is considerable erosion of the mucous membrane over both true and false vocal cords. The *trachea* is covered by a yellowish-gray necrotic membrane. Upon lifting the edge of this and stripping it back one has the impression of separating the mucous coat. The underlying surface is finely granular, with minute points of capillary hemorrhage. This membranous lesion extends down into the primary bronchi. The peribronchial glands are not enlarged. *Heart* normal. *Gastrointestinal tract* normal. Remaining organs show no significant lesions.

Microscopic examination.—*Skin:* The section shows definite necrosis, as evidenced by pink-staining cytoplasm, pyknosis of nuclei, vacuolization, separation of individual cells. There is loosening of the keratin lamellæ. The section passes through the edge of a vesicle filled with shreddy fibrinous coagulum. The separation appears to have taken place within the epidermis, and not between epidermis and corium. The superficial layer of the corium is moderately edematous and contains a few pycnotic wandering cells. There is no marked hyperemia; no thrombosis and no striking alteration of the vascular endothelium. *Primary bronchus:* Lined with a thick fibrinous membrane, in places distinctly laminated and containing polynuclear leucocytes, especially on the surface. The ciliated mucosa is still present beneath the membrane, though largely detached from the basal layer of cells. The nuclei of these detached cells are perhaps somewhat pycnotic, but there is no very evident necrosis. The membrane is attached at intervals by vertical fibrinous strands to the submucosa. The ciliated cells are separated from the basal row in places by fresh hemorrhage. The submucosa is very edematous, fibrinous, hemorrhagic, with moderate cellular infiltration. The mucous glands are flattened and do not appear to be actively secreting. *Medium-sized bronchus:* Shows similar changes, except that the lumen is completely filled by a loose fibrinopurulent exudate. An attached bronchial lymph node shows the sinuses filled with pus and fibrin. *Lungs:* There is marked subpleural and interlobular edema. The capillaries are universally congested. There is a patchy, very loose exudate into the alveoli, composed of well-preserved mononuclear and polymorphonuclear leucocytes, few erythrocytes, and occasional swollen and exfoliated epithelial cells. Two small bronchi in the section show an intact mucosa. There are scattered emphysematous vesicles. *Liver, spleen, kidney, pancreas, and adrenal* show no significant lesion.

Bacteriological report.—Blood culture (post-mortem) anaerobic media streptococcus hemolyticus, aerobic in second generation. Lung culture: Pneumococcus, type(?); micrococcus catarrhalis.

NOTE.—A very characteristic case of poisoning with mustard gas, probably dying on the second day after exposure. There were extensive skin burns, and a severe membranous necrosis of the upper respiratory tract. The lung showed an early patchy lobular pneumonia, with areas of edema. There are no features deserving special comment except, perhaps, the preservation of the tracheal epithelium, which is included in the fibrinous membrane.

CASE 10.—B. B., 2252004, Pvt., Co. A, 39th Inf. Died, October 14, 1918, 10.45 a. m., Base Hospital No. 58. Autopsy, October 15, 23 hours after death, by Capt. M. Flexner, M. C.

Clinical data.—Gassed October 11, 1918, admitted to Base Hospital No. 58 on same day. Semicomatose, no history obtainable. Tincture digitalis and oxygen inhalation.

Anatomical diagnosis.—Mustard-gas poisoning. Bronchopneumonia.

External appearance.—Cyanosis of face and ears. Two superficial blisters on forehead about 3 cm. in diameter. Superficial burn on bend of left elbow. No other cutaneous lesions.

Gross findings.—*Pleural cavities:* The right is free. The left is obliterated by old fibrous adhesions. *Pericardium:* Contains about 20 c. c. of clear fluid. *Heart:* Left ventricle is contracted; the right is flabby; no other lesions. *Right lung:* Has old fibrous adhesions between the upper and middle lobes. *Left lung:* The pleura presents a shaggy appearance

over both lobes. Lung feels cottony with the exception of a few calcified areas. In the upper lobe is a small patch of bronchopneumonia about 2 by 3 cm. In general the cut surface is dry, mottled pinkish red in color. Purulent bronchitis, somewhat less marked than in right lung. *Larynx, trachea, and large bronchi* are injected and contain thick yellow pus. *Gastrointestinal tract:* Normal. The remaining organs show no significant lesions.

Microscopic examination.—*Trachea:* The epithelium for the most part is desquamated. (This may be largely post-mortem, autopsy 23 hours after death.) In places there is a layer of squamous epithelium which seems to originate from the glandular ducts. There is a moderate leucocytic infiltration of the submucous tissue, with congestion and edema. The leucocytes in the superficial zone are caryorrhectic. Section through medium-sized bronchus shows complete necrosis of epithelium and formation of definite membrane. *Lung:* Terminal bronchioles and alveoli are filled with exudate composed of polynuclear cells. In some areas red cells predominate and moderate numbers of pigmented epithelial cells also are seen. There are small areas of emphysema and atelectasis. Alveolar capillaries are also congested. In sections stained by Gram method very few bacteria are seen. *Skin:* There is desquamation of the epidermis and remains of an old bleb. Slight leucocytic infiltration in subepithelial layer and some fibroblastic activity. There are a few polymorphic pigment cells.

NOTE.—A case of mustard-gas poisoning of three days' duration. Slight burns of skin; inflammatory changes of trachea and larger bronchi were rather superficial. No membrane except in smaller bronchi. Parenchyma of lung was very little affected.

CASE 11.—J. L. J., 2388735, Pvt., Co. M, 4th Inf. Died, October 17, 1918, 7 a. m., at Evacuation Hospital No. 6. Autopsy, three hours after death, by Capt. James F. Coupal, M. C.

Clinical data.—Mustard-gas burns and inhalation. Gassed on October 14. Area shelled daily with Yellow, Blue, and Green Cross shells; prolonged stay in contaminated vegetation and shell holes.

Anatomical diagnosis.—Multiple superficial burns of body with mustard gas. Acute ulcerative tracheitis and bronchitis. Bronchopneumonia. Acute fibrinous pleurisy.

External appearance.—Burns of face, scalp, conjunctivæ, left shoulder, arm, and axilla, scrotum, and buttocks.

Gross findings.—*Pleural cavities:* Contain each about 200 c. c. of clear fluid. Few fresh fibrinous adhesions. *Lungs:* Both present a similar appearance, showing alternating areas of emphysema, edema, and congestion. On section they yield quantities of dark blood and frothy fluid. Posterior portions are especially edematous; anterior margins emphysematous. *Organs of neck:* Base of tongue, fauces, pharynx and larynx are markedly congested. Moderate edema of glottis. *Trachea:* Throughout is denuded of mucosa. *Bronchi:* There is a loose membrane which extends from the trachea into the larger bronchi. Secondary bronchi contain purulent exudate.

Microscopic examination.—*Trachea:* There is an adherent fibrinopurulent slough in which is incorporated a necrotic submucosa. Coarse network of fibrin, with many distorted and fragmented nuclei and superficial masses of bacteria, composes the exudate. Here and there the surface is covered by a layer of flattened cells, the connection of which with the proliferating cells of the mucous ducts does not appear in the section. The fibrinous edema and leucocytic infiltration of the fibrous tissue extends quite deeply. There is extensive congestion but little or no hemorrhage. Some of the glands show excessive mucous secretion; others are exhausted. *Lung:* Bronchi are filled with purulent exudate. Epithelium is largely preserved. Wall moderately congested and hemorrhagic. There is a fine fibrinous exudate in the surrounding alveoli. In these plugs of exudate are large well-preserved epithelioid nuclei, probably derived from alveolar cells. The alveolar epithelium under the immersion shows interesting changes. It is swollen and vacuolated. In many places there is an active growth of epithelial cells which creep along the alveolar walls or follow fibrin strands to invade or cover the plugs of exudate. In these places one finds the remains of the original epithelial lining. This epithelial reaction is the most striking feature of the section. *Liver and spleen* show no lesions of interest.

NOTE.—Case of typical mustard-gas poisoning, with extensive diphtheritic necrosis of trachea and bronchi and characteristic peribronchial reaction. There were interesting regenerative changes in the alveolar epithelium.

CASE 12.—J. R., 134681, Pvt., Co. B, 102d F. A. Died, October 13, 1918, 3 p. m., Evacuation Hospital No. 6. Autopsy No. 54. Autopsy, October 14, 19 hours after death, by Capt. James F. Coupal, M. C.

Clinical data.—Exposed on 9th and 10th of October to gas shelling (mustard gas and chloropierin) over a period of five and one-half hours, 2,000 105-mm. and 150-mm. shells used over small area. Masks were removed too soon and soldiers slept in a gassed area. Diagnosis of mustard-gas poisoning.

Anatomical diagnosis.—Multiple mustard-gas burns of skin; acute ulcerative tracheitis; purulent bronchitis; bronchopneumonia; fibrinous pleurisy; acute parenchymatous nephritis.

External appearance.—Burns of face, neck, conjunctivæ, corneæ, elbows, axillæ, and scrotum.

Gross findings.—*Pleural cavities:* Lungs retract very slightly on opening the thorax. The right contains 400 c. c. of fluid with many fresh fibrinous adhesions.

(The following note was dictated at the pathological laboratory, Experimental Gas Field.)

Respiratory organs.—*Trachea and bronchi* are intensely congested. There is no membrane. *Right lung:* The upper lobe is voluminous and congested and markedly edematous. Middle lobe shows confluent lobular consolidation, affecting the entire lobe, with much fibrinous exudate about the pleural surface. The lower lobe shows extensive pneumonic consolidation, confluent in the lower portion. *Left lung:* Both upper and lower lobes are moderately congested and edematous and are free from pneumonic consolidation. *Alimentary tract:* Not examined. *Kidneys:* Cortex is mottled, alternately pale and hemorrhagic. The capsule is somewhat adherent. Vessels engorged. The remaining organs show no significant changes.

Microscopic examination.—*Trachea:* Shows complete loss of epithelium, with necrosis of the superficial portion of the submucosa. Associated with the leucocytic invasion, there is a fibrinous exudate and capillary hemorrhage. Nuclei of leucocytes show marked karyorrhexis. There is no false membrane. Epithelium of the ducts is conserved and in part widened. Mucous glands are degenerating. *Bronchus:* There are a few shreds of apparently proliferating epithelial cells beneath the fibrinopurulent membrane. Edema is intense. The bronchial wall is congested and there is early proliferation of the fibroblasts. *Lung:* Alveoli are very large. Many are partially filled with dense leucocytic exudate. Some edema of the interlobular septa and about the bronchi. There is also patchy alveolar edema. In the nonconsolidated areas there is marked congestion, with extensive exfoliation of the alveolar epithelium. Gram-stained section shows many Gram-positive cocci, morphologically staphylococci, occurring in groups in the alveolar exudate. *Kidney:* Shows acute hemorrhagic nephritis. There are no inflammatory lesions in the glomeruli. There is considerable epithelial necrosis, some of which may be autolytic. *Liver and spleen* show no significant lesions.

NOTE.—The lesions are sufficiently typical of early mustard-gas poisoning (duration 3 days) except for the presence of an acute hemorrhagic nephritis. It is interesting to note that McNec recorded one case of hemorrhagic nephritis in his series of 18 mustard-gas cases.

CASE 13.—A. J. L., 1426227, Cpl., Co. G, 30th Inf. Died, August 13, 1918, at 3.30 p. m. at Base Hospital No. 27. Autopsy, one and one-half hours after death, by Capt. H. H. Pernar, M. C.

Clinical data.—August 10, admitted to Field Hospital No. 7. Diagnosis: Exposure to mustard gas. Eyes irrigated; soda bath. Transferred at 6.30 p. m. to Evacuation Hospital No. 6. August 12, admitted to Base Hospital No. 27. Surface burns of back and genitals, edema of lungs, rapid, weak heart. August 13, died at 3.30 p. m. *Clinical diagnosis:* Inhalation of deleterious gas, mustard gas and phosgene (?).

Summary of gross lesions.—Excoriations and second-degree burns of skin back and genitals. Both pleural cavities empty. *Left lung:* Weighed 960 grams; upper lobe congested and edematous, lower lobe shows peribronchial consolidation. *Right lung:* Weighed 70 grams; areas of consolidation in all lobes, which are markedly congested. Completed destruction of mucosa of primary bronchi. Right side of heart dilated.

Microscopic examination.—*Trachea and large bronchi:* No material preserved. *Lung:* The medium-sized bronchi show complete epithelial necrosis, with the formation of fibrinopurulent plugs, in some cases occluding the entire lumen. The epithelium in a few of the bronchi shows early regeneration. The bronchioli have an intact epithelium, normally ciliated, but contain purulent exudate. So also the atria. The lung tissue itself is the seat of confluent lobular pneumonia, the exudate in places being cellular, in others more fibrinous. There are no distinctive features.

NOTE.—An incompletely studied, but apparently typical case, of mustard-gas poisoning of three days' duration. There is nothing in the findings at autopsy to confirm the clinical suspicion of exposure to phosgene in addition to mustard gas.

CASE 14.—J. M. P., 1630061, Pvt., Co. H, 30th Inf. Died, August 13, 1918, at 2 p.m. at Base Hospital No. 27. Autopsy No. 30, performed one and one-half hours after death by Capt. H. H. Permar, M. C.

Clinical data.—Gassed with mustard-gas shells at Chateau Thierry on August 10; admitted to Field Hospital No. 7 on same day. Eyes irrigated with novocaine; soda bath. August 12, admitted to Base Hospital No. 27. Extremely cyanotic and dyspneic; weak, rapid pulse; burns over entire body surface. *Lungs:* Moist râles throughout.

Summary of gross lesions.—Large blebs over back, chest, arms, face, and genitals. Few old adhesions in right pleura, left negative. *Left lung:* Weight, 466 grams; scattered areas of emphysema, atelectasis and consolidation in lower lobe; upper lobe congested. Bronchi filled with crust-like yellow slough. *Right lung* weighs 530 grams; voluminous, emphysematous, areas of consolidation in lower lobe. *Trachea* ulcerated and covered with pseudo-membrane. *Right heart* dilated. Old tuberculous lesions in peribronchial lymph-node.

Microscopic examination.—*Medium-sized bronchus:* There is complete denudation of the epithelium; the wall is formed by a dense granulation tissue, with distorted nuclei of inflammatory cells. No membrane is included in the section. The mucous glands are atrophic. *Lungs:* The smallest bronchi are filled with purulent exudate; their epithelium is intact. The alveoli contain a dense cellular exudate, the pneumonic process being diffuse and confluent. There are no special features.

NOTE.—An incompletely described case of early mustard-gas poisoning of three days' duration showing the usual findings at autopsy.

CASE 15.—A. L., 547297, Pvt., Co. H, 30th Inf. Died, August 13, 1918, at 5.30 a. m., at Base Hospital No. 27. Autopsy No. 29, performed three and one-half hours after death, by Capt. H. H. Permar, M. C.

Clinical data.—August 10, exposed to mustard-gas shelling. Admitted to Field Hospital No. 7. August 12, admitted to Base Hospital No. 27, with diagnosis of mustard-gas inhalation and contact burns of extremities, head, and back. Cardiac failure.

Anatomical diagnosis.—Burns of face, shoulders, back, chest, arms, thighs, and knees; pigmentation of skin of scrotum; laryngitis, tracheitis, and bronchitis, mucopurulent, with sloughing of mucosal lining; bronchopneumonia, early bilateral; edema and congestion of lungs. *Heart:* Dilatation of right side.

Microscopic examination.—*Trachea:* There is complete destruction of the surface epithelium, but that of the ducts of the mucous glands is intact, and already actively proliferating. There are small shreds of false membrane adherent in places, but in general the trachea is lined by the necrotic submucous tissue. The zone of necrosis extends to the mucous glands, and the membrana propria is destroyed. In the necrotic tissue are many wandering cells, with pyknotic and distorted nuclei. The blood vessels are intensely congested. The glands appear somewhat compressed and flattened. *Medium-sized bronchus:* About the same picture as in the trachea. In one area, the necrotic epithelium, the cells of

which have completely lost their staining, is lifted up from the membrana propria by a collection of leucocytes, forming a sort of pustule. A *smaller bronchus* shows in addition very extensive hemorrhage into the deeper portion of the submucosa. *Lung:* Bronchioli show a suppurative inflammation, but their epithelium is still intact. There is an extensive lobular pneumonia, without special features. The exudate is very cellular, and the leucocytes well preserved.

NOTE.—A very severe but typical case of mustard-gas poisoning of only three days' duration. An interesting point in the histological study of the trachea is the early proliferation of the epithelium of the mucous ducts.

CASE 16.—H. B., 2193795, Pvt., 314th F. S. B. Died, August 11, 1918, at Base Hospital No. 116. Autopsy by Lieut. B. S. Kline, M. C.

Clinical data.—Gassed with mustard-gas August 7; admitted to Base Hospital No. 116 on August 10, with cyanosis and extensive edema; severe burns all over body. Right heart dilated. Pulse rapid and weak. Treated with stimulants and venesection.

Anatomical diagnosis.—Extensive gas burns, upper respiratory tract. Superficial burns of skin, penis, and scrotum. Acute seropurulent conjunctivitis. Pigmentation of skin of face and scalp. Ulceration of mucosa of larynx, trachea, and bronchi. Acute membranous laryngitis, tracheitis, and bronchitis. Bronchopneumonia. Acute lymphadenitis. Cloudy swelling of parenchymatous organs. Cardiac dilatation, right side, moderate. Pulmonary edema, slight.

External appearance.—Body is that of an adult male, 192 cm. in length, well developed. Rigor is present to a considerable degree in the voluntary muscles. There is a moderate amount of hypostasis. In the skin of the back, particularly over the left shoulder and left axilla and to a less extent over the right scapular region; above this and between the scapulae there are large superficial ulcerated areas. The base is clean and has a reddish-brown appearance. There is a similar smaller ulcerated area in the left lumbar region. There are others about the sacrum, the axilla on each side, the right upper arm, and over the chest anteriorly, particularly in the region of the ensiform. There is also superficial ulceration about the prepuce, the anterior surface of the scrotum showing a matted scab. These ulcerations are very superficial and extend into the dermis only. At the bend of the left elbow there is an area of vesiculation several centimeters in length and about 6 mm. in width. There is also another area on the left greater trochanter, a few centimeters in diameter. At the bend of the right elbow there is a superficial ulcerated area similar to those described above, and in addition over the head of the ulna there is an area of contusion. The skin of the face and scalp have a brownish color. There are beginning vesicles about the left side of the mouth. The inguinal glands are somewhat enlarged. The mucous membranes are pale. *Eyes:* The eyelids are somewhat swollen, the lids glued together by tenacious mucopurulent material. The conjunctivæ are edematous and there are patches of injection of the bulbar conjunctiva. There is a slight cloudiness of the cornea. The pupils, about 3 mm. in diameter, equal. *Nose:* In the nose there is a moderate amount of mucopurulent material. *Mouth:* No abnormalities. *Chest:* Well formed, costal angle about 90°. *Abdomen and extremities:* Natural looking.

Gross findings.—*Pleural cavities:* On opening the thorax the right pleural sac is free of fluid and adhesions. The left pleural sac is likewise free of fluid and adhesions. The heart lies in normal position. On incising the pericardial sac no abnormalities of or in the sac are visible. On the ventral surface of the right ventricle there is typical milky patch. *Heart:* Right auricle and ventricle moderately dilated. Otherwise normal. *Right lung:* All lobes voluminous, cushiony, somewhat soggy, palpable solid areas here and there, most marked in the upper and median portion of the upper and middle lobes. The glands at the hilus are somewhat enlarged, pulpy, pigmented, and somewhat injected. *Bronchus:* The mucosa in the greater part ulcerated. Covering the denuded submucosa there is an elastic fibrinous membrane forming a cast of the bronchial tree. The vessels at the hilus show no abnormalities except perhaps some dilatation of the arteries. On section of the upper lobe a moist pinkish-red surface presents. The tissue is quite well aerated. In the air sacs there is a moderate amount of thin frothy fluid. Medially there are vaguely outlined grayish-red solid patches varying in size from a few millimeters to a few centimeters in diameter. Posteriorly the solid patches are fewer in number and the tissue is well aerated. The middle lobe on section crepitates.

Medially there is a large walnut-sized, solid, dull reddish-gray patch. Nearby there are other solid patches of similar appearance. In the smaller bronchioles in this lobe viscid purulent exudate is visible. There is one peribronchial lymph node, grape seed in size, surrounded by a firm pigmented zone. On section of the lower lobe the tissue crepitates. The tissue is well aerated. In the air sacs there is a small amount of thin frothy fluid. The tissue is somewhat congested. In the large bronchial branches there is an adherent mass of exudate. On repeated section no definite solid areas can be made out. *Left lung:* The glands, vessels, and bronchi similar in appearance to those on the right. The pleura here, as on the right side, is thin and delicate. The lobes, as of the right, are very voluminous, cushiony. On section they crepitate. In the median portion there are good-sized reddish, dull gray areas of consolidation. In the left lower lobe the purulent exudate in the bronchioles is striking in amount. *Neck organs:* The larynx is filled with tenacious viscid mucopurulent exudate, most marked in the epiglottis and about the true vocal cords. The pouch behind them likewise is filled with a viscid exudate. The trachea is similar in appearance except that the exudate lessens in amount toward the bifurcation. Here the patchy ulceration of the mucosa is very striking. Below it the submucosa is intensely injected. Attached to the tip of the epiglottis there is an adherent elastic, friable plug of exudate. Throughout the upper respiratory tract the submucosa and the muscular coats are considerably edematous. The thyroid of average size and consistency. On section the tissue is spongy. The acini contain but a small amount of colloid. The tonsils of fair size and project somewhat above the general level. On section the tissue in great part is scarred. There is but a small amount of lymphoid tissue present. The crypts are clean. *Alimentary tract:* The upper end of the esophagus and the base of the tongue show considerable injection of the mucosa. There is no ulceration present, however, and no exudate. The stomach contains some intensely bile-stained contents and a small amount of mucus. In the mucosa there are scattered areas of patchy injection. The duodenum shows no abnormalities. In the lower ileum there are patches of patchy injection of the mucosa. The solitary follicles are somewhat more prominent than normal in the lower ileum. Patchy injection of the cecum and of the transverse and descending colon. The appendix shows considerable patchy injection of the mucosa with tiny hemorrhages, especially marked in the tip. *Kidneys* show cloudy swelling.

Microscopic examination.—*Lungs:* No large bronchi are included in the sections. There is dilatation and hyaline necrosis of the walls of the infundibula. Small bronchioles still retain their epithelium but their walls are infiltrated with inflammatory cells. Alveolar walls are congested and contain many leucocytes. There is typical bronchopneumonia, the exudate being composed chiefly of well-preserved polymorphonuclear leucocytes. There is very little fibrin. *Trachea:* Well-formed laminated membrane invaded with leucocytes and containing in one area a large mass of mucus. Beneath the membrane in places a single row of epithelial cells with pyknotic distorted nuclei. Marked swelling of membrana propria. Edema, congestion, hemorrhage, and leucocytic infiltration of submucosa. The ducts of the mucous glands are distended with thick plugs of mucus. The epithelium in the superficial portion is destroyed. (Fig. 28.)

Bacteriological report.—Smears made from the exudate in larynx show innumerable organisms. The predominating one, a Gram-positive lancet-shaped diplococcus. In addition there are some rounded Gram-positive cocci, also a moderate number of small and large Gram-negative bacilli and a few Gram-negative cocci.

NOTE.—A typical case of mustard-gas poisoning of four days' duration. There was a diphtheritic tracheobronchitis, with patches of secondary bronchopneumonia. Histologically the lung lesions differ from the influenzal pneumonias in the absence of extensive hemorrhagic edema and in the presence of large numbers of leucocytes in the exudate. There was, however, hyaline necrosis of the walls of the dilated atria, such as was commonly observed in the influenzal pneumonias.

CASE 17.—A. H., 1940705, Pvt., Co. E, 20th Inf. Died, October 7, 1918, Gas Hospital A. Autopsy, October 8, four hours after death, by Lieut. Russell W. Wilder, M. C.

Clinical data.—Gassed on October 3, 1918. Burns of skin, eyes, and respiratory tract.

Anatomical diagnosis.—Hyperemia of mucous membranes of larynx, pharynx, and trachea. Ulcerations of mucous membrane of bronchi. Emphysema and beginning atelectasis of lungs. Healed apical tuberculosis. Parenchymatous degeneration of liver and kidneys. Second-degree mustard-gas burns of face, arms, and trunk.

External appearance.—Moderate cyanosis and lividity. Large vesiculated burns of arms and trunk. Desquamation of skin of scrotum, leaving raw bloody surface. Purulent discharge from eyes.

Gross findings.—*Lungs:* Distended. No free fluid in pleural cavities. Pleura is smooth and glistening. Right, crepitates throughout. On section reveals small bronchi occluded with fibrinous exudate. Larger bronchi covered by membrane, which, when stripped away, reveals longitudinal muscle fibers. Extensive areas of emphysema and other areas of beginning atelectasis. Left, shows similar picture. There is a calcified scar 1 cm. in diameter in the apex of the upper lobe. *Heart:* Right ventricle moderately dilated. Mitral orifice somewhat stenotic, showing old endocardial scars. *Abdomen:* Adhesions about the site of old appendectomy. *Gastrointestinal tract* not examined. *Pharynx* intensely congested. *Larynx* and *tracheal mucosa* hyperemic, but not ulcerated or covered by exudate. Thin purulent material in tracheal lumen.



FIG. 28.—Case 16. Mustard-gas burn, 4 days' duration. Trachea. Low-power view, showing laminated false membrane attached to openings to mucous ducts

Microscopic examination.—*Trachea:* Tissue poorly preserved. Epithelium desquamated. Submucous layer is edematous, congested, and infiltrated with leucocytes. There is no pseudomembrane. Section of medium-sized bronchus shows complete destruction of mucosa, with formation of false membrane composed of laminated fibrin. *Lung:* Sections unsatisfactory. Show only congestion of capillaries and desquamation of mononuclear epithelial cells.

NOTE.—A typical early case of mustard-gas poisoning, dying four days after exposure. There was a membranous inflammation involving the bronchi, more deep seated than that in the trachea and extending into the smallest branches. Parenchyma of the lung, aside from the emphysema and atelectasis, due to occlusion of the bronchi was very little affected.

CASE 18.—C. P., 3171057 (rank and organization not given). Died, October 13, 1918, 11 a.m., Evacuation Hospital No. 6. Autopsy No. 53. Autopsy, October 14, 27 hours after death, by Capt. James F. Coupal, M. C.

Clinical data.—Gassed October 7 or 8. Died while being evacuated. Diagnosis: Mustard-gas poisoning.

Anatomical diagnosis.—Multiple superficial burns. Acute ulcerative tracheitis; purulent bronchitis; bronchopneumonia; acute fibrinous pleurisy; acute parenchymatous nephritis.

External appearance.—Burns of face, neck, conjunctivæ, cornea, scrotum, buttoek, and thighs. Multiple blisters. Marked subcutaneous emphysema at base of neck and extending down to first rib. Paraphimosis.

Gross findings.—*Pleural cavities:* Lungs retract very slightly. Left pleural cavity contains 100 c. c. of sterile yellow fluid. Right, a similar amount, with few fibrinous adhesions over the diaphragm. *Heart:* The right ventricle is dilated.

(Note dictated at the pathological laboratory, experimental gas field.) *Respiratory organs.*—*Trachea:* Covered with tough continuous membrane extending into the smaller bronchi. The anterior portions of both lungs, including the right middle lobe, are emphysematous, while the posterior portions are congested and edematous. There are no gross pneumonic lesions. *Alimentary tract:* *Intestines* injected throughout. The remaining organs show no significant lesions.

Microscopic examination.—*Trachea:* Has a well-formed pseudomembrane composed of fibrin infiltrated with polymorphonuclear leucocytes. Submucous layer is congested, edematous and infiltrated with wandering cells, showing beginning caryorrhexis. An interesting point is the presence over large areas of a single row of epithelial cells beneath the pseudomembrane and still attached to the swollen membrana propria. The leucocytic infiltration is not dense. There is beginning caryorrhexis and capillary extravasation. The mucous glands do not appear to be in active secretion. *Branchus:* Section through a medium-sized bronchus shows complete necrosis of the epithelium. The lumina are filled with purulent exudate. *Lungs:* There are a few small bronchi in the section showing generally exfoliation of the epithelium, probably post-mortem. The alveolar capillaries are congested, tortuous, and contain an increased number of polymorphonuclear and large mononuclear cells. A few air spaces are collapsed, others contain pink coagulum. There is slight exfoliation of the alveolar cells. No pneumonia. *Skin:* The epithelium is raised up from the corium in a continuous sheet, forming a blister, the contents of which consist of homogeneous, slightly fibrinous coagulum with a fair number of leucocytes, chiefly polymorphonuclears. The epithelial cells show varying degrees of necrosis. The underlying corium is moderately edematous and loosely invaded by wandering cells. The vessels are not extremely congested and are free from thrombi even in the superficial zone. Near the surface there are small irregular cells containing pigment, some of which seem to have been derived from the basal cells of the rete mucosum. Some of the brown pigment has been taken up by the polymorphonuclears. At the margin of the blister the epidermal cells are in places detached from their neighbors, and there is considerable leucocytic infiltration, especially in the zone just above the pigment layer. Papillary processes are edematous. (See fig. 6.)

NOTE.—Mustard-gas case, five or six days' duration. There was a typical membranous tracheobronchitis, in addition to the typical cutaneous lesions. The pulmonary parenchyma, according to the gross description and the single histological block available, showed only emphysema, edema, and congestion. There was no pneumonia.

CASE 19.—D. B., 187, Pvt., 1/4 Highlanders R. Died, October 23, 1918, at 5.10 a. m., at Base Hospital No. 2. Autopsy, four and one-half hours after death, by Maj. A. M. Pappenheimer, M. C.

Clinical data.—October 20, admitted to No. 5 Casualty Clearing Station, with diagnosis of shell-gas poisoning (irritant). October 22 admitted to Base Hospital No. 2. Patient is pale; breathing with much difficulty; edematous; pulse 140, very weak; blood pressure 120–100. No sounds during respiration. Sputum mucopurulent. *Chest:* Good resonance, tracheal and bronchial râles. *Heart:* Cardiac dullness within normal limits. Patient received an intravenous dose of strophanthin at 7 p. m. Oxygen administered, October 23, 4 a. m. Pulse very weak; pale; thirsty. Died at 5.10 a. m.

Anatomical diagnosis.—Membranous tracheobronchitis; lobular pneumonia; congestion and edema of lungs; pleural adhesions; acute conjunctivitis; congestion of viscera.

External appearance.—Conjunctivæ are injected, slightly more so on left side. Abundant thin watery fluid flowing from mouth. The mucous membrane over the lower lip is a little macerated. There are no burns or other cutaneous lesions.

Gross findings.—*Pleural cavities:* On both sides obliterated by organized adhesions. Lungs meet in median line to third interspace. *Lungs:* Voluminous and heavy, covered everywhere with edematous sheet-like adhesions. In all lobes there can be felt firm areas which are quite extensive. *Right lung:* On section, upper lobe shows very widespread areas of consolidation, which are grayish red and granular, forming patches 2 or 3 cm. in size, between which the lung tissue is very edematous and congested. The bronchi are thick, the larger ones lined with a continuation of the gray membrane present in the upper respiratory passages, the smaller ones completely filled with purulent fluid. In the lower and middle lobes the consolidation is less extensive but of the same character. The bronchi are surrounded by a sunken red zone. *Left lung:* Presents a similar picture. The most extensive consolidation is in the lower lobe, about two-thirds of which are completely consolidated. *Organs of neck:* Tongue normal. Tonsils small, normal on section. The pharynx congested, slight thickening of the arytenoepiglottidean folds. On the laryngeal surface of the epiglottis the mucous membrane in places is denuded and covered by a thin grayish membrane. The vocal cords and the entire lining of the trachea and primary bronchi are covered with a coherent, rather moist yellowish-gray membrane. This is readily detached, leaving a swollen red velvety surface, apparently covered by epithelium. *Esophagus* normal. *Heart* normal. Remaining viscera, including gastrointestinal tract, show no significant changes.

Microscopic examination.—*Trachea:* There is no membrane preserved in the section. The epithelium is reduced to occasional small groups of flattened cells, with pyknotic nuclei. The membrana propria is swollen. The submucous tissue is the seat of fibrinous edema. There is congestion, scattered hemorrhage, and loose inflammatory infiltration. The leucocytes as they approach the surface show pycnosis and karyorrhexis. The edema extends through the wall of the trachea to the neighboring fat and areolar tissue. *Primary bronchus:* The section shows a loose fibrinous membrane, to the base of which are attached strips of exfoliated epithelium. There is a curious arrangement of the fibrin. To the swollen membrana propria, are still adherent in places, flattened, deeply staining epithelial cells. The openings of the mucous ducts are dilated with mucus and exfoliated cells. The edema, congestion, hemorrhage, and leucocytic infiltration of the bronchial wall are like that in the trachea. *Tonsils:* No epithelial necrosis. *Lungs:* Bronchi filled with purulent exudate which in the terminal infundibula are in the form of fibrinopurulent plugs completely filling them. The epithelium is preserved in part. There is diffuse pneumonia, showing no special features. The exudate is rich in polymorphonuclear leucocytes, showing early pycnosis. The capillaries are extremely congested, and there is moderate diapedesis. There is rather marked periarterial edema. Another block shows a medium-sized bronchus, cut longitudinally and completely occluded by a fibrinopurulent plug. A few flattened epithelial cells persist here and there where the plug is less firmly attached. The wall is edematous and loosely invaded by wandering cells. The rest of the section shows edema, patchy in distribution, emphysema, and congestion. *Liver, spleen, pancreas, and adrenals:* Show no special features.

Bacteriological report.—Blood culture (post-mortem) anaerobic streptococcus, dying on transplant. *Staphylococcus aureus.* *Lung culture:* *B. influenzae* and pneumococcus, Type IV.

NOTE.—This case, probably one of mustard-gas poisoning of three or four days' duration, is interesting and unusual because of the absence of cutaneous lesions. The diphtheritic necrosis of the trachea and bronchi were very severe and extensive and could hardly be ascribed to an influenzal infection alone. There was, moreover, a definite history of shell-gas inhalation. The eye lesions appear to have been very mild.

CASE 20.—J. A. A., 1681974, Pvt. (Co. not given), 306th Inf. Died, September 29, 1918, at Base Hospital No. 18. Autopsy No. 99, performed 16½ hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Gassed on the night of September 25. Died shortly after admission to Base Hospital No. 18. No further data are available. The records at hand show four other casualties from gas on the night of September 25 in the 306th Infantry. One thousand five hundred 77 and 105 mm. Yellow Cross shells were used in the bombardment, which lasted one hour.

Anatomical diagnosis.—Gas burns of scrotum, conjunctivæ, and respiratory tract; infected scrotal burn; acute conjunctivitis; acute esophagitis; laryngitis, tracheitis, and bronchitis; peribronchial and bronchopneumonia; acute lymphadenitis, regional lymph nodes; healed pleural adhesions; pulmonary edema, slight to moderate; chronic diffuse nephritis; myocardial scars, left; hypertrophy of left ventricle, considerable; anemia and emaciation, slight to moderate.

External appearance.—The skin is thin and sallow. The scrotum shows an area of superficial necrosis of the epidermis over each testis, also in the midline, several centimeters in diameter. Over this there is matted serum and a small amount of purulent exudate. The superficial lymph glands are palpable. The conjunctivæ are diffusely injected. There is a small amount of fibrinopurulent secretion present; both corneæ are cloudy. There is superficial ulceration of the mucosa of the lips, covered with sores; many teeth poorly formed.

Gross findings.—*Pleural cavities:* Right pleural sac obliterated by sheetlike adhesions. On the left side, no abnormalities. *Right lung:* All lobes are voluminous, except the middle lobe, which is smaller than the average. The pleura in general is thickened. The lobes are bound to each other and to the pericardium by fibrous bands. Vessels at the hilum are normal. The lymph glands are enlarged, pulpy, injected, and edematous. The bronchus shows a striking picture; there is injection of the mucosa with patches of ulceration; in many places fibrinous and fibrinopurulent exudate adheres to the walls. On section of the upper lobe the tissue in the posterior part shows slight congestion and moderate edema. Throughout the lobe there are scattered areas of peribronchial consolidation, varying in size up to a few centimeters in diameter. In general they average only several millimeters. The middle lobe in its greater portion shows a patchy grayish-pink consolidation; about two-thirds of the lobes are involved. The right lower lobe on section resembles the upper. There is more uniform congestion, and the consolidation is more distinctly peribronchial. The bronchial branches throughout this side contain tightly adherent fibrinopurulent exudate. *Left lung:* Also voluminous in both lobes. The entire lung, except the apex of the upper lobe feels soggy and solid. Over the lower lobe posteriorly there is a small amount of fibrinous exudate. Glands at the hilum, vessels and bronchi are similar to those on the right side. On section of the upper lobe the upper part is well aerated and pink, but contains a few bronchopneumonic areas. In the lower portion there is considerable edema, slight congestion, and scattered areas of grayish consolidation, peribronchial and pneumonic. In the median portion of the lobe there is an area of consolidation several centimeters in diameter; the consolidation here is almost uniform grayish and red, finely granular. The lower lobe on section presents a picture similar to the lower portion of the upper, but is more extensive. The smaller bronchial branches are like those on the right side. *Organs of neck:* The larynx is lined with a necrotic white mucosa, covered in great part with tenacious, yellowish, slightly green tinged, coherent exudate. The true vocal cords and lower portion of the larynx are especially affected. A similar condition is present throughout the trachea, although the exudate is somewhat less abundant. Patchy injection and superficial ulceration of the mucosa is visible here and there. The posterior wall of the pharynx and the upper esophagus present a picture like that in the upper part of the larynx. The tonsils are slightly enlarged, edematous, pale, and scarred. *Heart:* Weighs 320 grams, the left ventricle about twice the average thickness. There are myocardial scars, and the muscle is coarse in texture. Sclerotic patches are seen in the coronaries and at the base of the aorta. *Kidneys:* Reduced in size and show irregular atrophy of the cortex and indistinct markings. *Gastrointestinal tract:* Not described. Remaining viscera show no changes of interest.

Microscopic examination.—*Trachea:* Longitudinal section cut. There is complete epithelial necrosis. Masses of tightly adherent fibrinopurulent exudate, in which are many bacterial colonies, cover the surface. The submucous tissue is only superficially infiltrated with inflammatory cells. The tissue is poorly preserved, and the red cells in the vessels are not stained. *Pharynx:* On the surface is an adherent fibrinopurulent slough; there is edema, intense congestion and inflammatory infiltration of the submucous tissue. *Lungs:* The smaller bronchi are lined with adherent fibrinopurulent exudate which is incorporated in the wall and does not form a distinct membrane. The terminal bronchioles and infundibula are filled with pus; their epithelium is still partially preserved. The parenchyma shows a diffuse pneumonia; the exudate is of varying composition, in places almost fibrinous, in others containing dense aggregations of leucocytes. There are no features of special interest.

The finer details are somewhat obscured by formalin pigment. Another section shows circumscribed areas of pneumonia, in which there is great fragmentation of leucocytes and abundant bacterial growth. The appearance suggests beginning gangrene. Some of these consolidated foci are surrounded by zones of hemorrhagic edema. There is marked perivascular edema in some sections.

NOTE.—Typical early case of mustard-gas poisoning, of four days' duration, with severe diphtheritic necrosis of the upper respiratory passages.

CASE 21.—A. B., 240806, Pvt., Co. L, 309th Inf. Died, October 22, 1918, at 2.20 p. m., at Base Hospital No. 15. Autopsy (time not given) by Maj. Daniel Glomset, M. C.

Clinical data.—Gassed (inhalation and contact) October 17, 1918. October 20, diagnosis of lobar pneumonia right lower lobe was made.

Anatomical diagnosis.—Bronchopneumonia, all lobes, pseudomembranous tracheitis and bronchitis. Parenchymatous degeneration of liver and kidneys. Second-degree burns of skin. No detailed description of gross lesions available.

Microscopic examination.—*Trachea:* The membrane, only shreds of which are present, consists of coarse fibrin network in which are scattered pyenotic leucocytes. Surface is formed by the slightly swollen basement membrane. The outer half of the submucosa is necrotic. There is a coarse fibrinous exudate in the edematous tissue with deeply staining nuclei. Vessels are congested but there is no hemorrhage. The mucous ducts are apparently obstructed at their orifices. They are dilated, as are many of the mucous glands, and the epithelium is metaplastic, in places showing regenerative changes. *Lungs:* There are small patches of pneumonia definitely grouped about the bronchioles and atria, in which are found the usual lesions. Uninvolved lung is emphysematous. *Kidney, myocardium, and adrenals* show no lesions of interest.

NOTE.—Typical case of mustard-gas poisoning of five days' duration, with membranous tracheobronchitis. Lesions of the lung parenchyma are sharply limited to the peribronchial regions. It is of interest to note that regenerative changes in the epithelium of the mucous ducts are already in progress.

CASE 22.—S. D., 2250618, Pvt., Co. I, 39th Inf. Died, October 16, 1918, 8.30 a. m., at Base Hospital No. 59. Autopsy No. 7. Autopsy, four and one-half hours after death, by Capt. M. Flexner, M. C.

Clinical data.—Gassed October 11, 1918. Exposed to blue, green, and yellow cross shells. Admitted to Field Hospital the same day. Base Hospital No. 59 on October 13. On admission, conjunctivitis, sore throat, pain in chest, râles of all types throughout chest. Diagnosis of gas inhalation and bronchopneumonia.

Anatomical diagnosis.—Mustard-gas burns. Fibrinopurulent tracheo-bronchopneumonia. Acute fibrinous pleurisy. Emphysema.

External appearance.—Skin about eyes, nose, and mouth shows crusts from gas burns. Scrotum shows dense scab formation from old burns, and other severe superficial burns on the elbows. Eyes show conjunctivitis, bilateral keratitis. Cornea have steamed appearance.

Gross findings.—*Pleural cavities:* *Right lung:* Pleural surface is shaggy anteriorly, due to fibrous adhesions. There are more recent adhesions between the visceral pleura and the pericardial sac. Upper lobe is grayish white in color with a few darker patches, especially at the apex, and the lobe has a cottony feeling. On section, it is a pinkish-gray color with scattered flesh-colored areas from one-half to 3 cm. in diameter. On pressure bloody, frothy fluid escapes. The base of lower lobe is firm and darker in color. Excised piece of darker tissue sinks when placed in water. *Left lung:* Pleura over lower lobe is covered with fibrous tags. Upper lobe, on section, is pinkish gray in color. Contains scattered flesh-colored areas. Around smaller bronchioles are narrow dark colored zones. The upper two-thirds of the lower lobe are reddish brown with a few scattered purplish areas, which are dry and granular and apparently contain no air. Lower lobe is pinkish gray in color with few scattered elevations. *Trachea* and larger bronchi show erosions of mucous membrane, with fibrin. The remaining viscera show nothing of interest.

Microscopic examination.—*Trachea:* In the trachea is deep-seated necrosis, which involves the epithelium and underlying tissue to a considerable depth. Incorporated in this necrotic area is a dense fibrinous membrane infiltrated with many pycnotic leucocytes, and in a few places there are clefts which separate the membrane of dead tissue from the underlying living tissue, and these are lined with flattened cells, possibly derived from the remains of the epithelium. There is extreme distension of all the blood vessels which form wide sinuses almost like a cavernous angioma. The mucous glands are compressed and distorted. (See fig. 13.) *Lungs:* The picture is unusual. There is an extensive hemorrhagic and fibrinopurulent exudate in the alveoli, the arteries of which are rendered indistinct by the fragmentation of the nuclei and the abundance of chromatin debris in the septa. (See fig. 23.) The elastic framework is torn and disrupted, as can be seen in appropriately stained sections. There is great edema of the interstitial tissue and the interlobular septa. There are masses of Gram-positive bacteria scattered through the section.

NOTE.—Case of mustard-gas poisoning of five days' duration. There was the usual diphtheritic necrosis of the upper respiratory passages. Pneumonic lesions of the hemorrhagic "influenzal" type, with infarct-like areas of necrosis.

CASE 23.—J. B., 2810342, Pvt., Co. C, 344th M. G. Bn. Died at 6 p. m., October 7, 1918, Justice Hospital Group, Toul. Autopsy No. A9. Autopsy performed, 19 hours after death, by Capt. Jean Oliver, M. C.

Clinical data.—Severe mustard-gas intoxication, incurred October 2, 1918.

Anatomical diagnosis.—Pigmentation of skin of face; suppurative and hemorrhagic tracheobronchitis; congestion and edema of lungs; interstitial emphysema.

External appearance.—The skin over face is brown. The epithelium is excoriated in small areas and can be rubbed off on pressure. No typical mustard-gas burns. Skin of scrotum shows similar changes. No other cutaneous lesions.

Gross findings.—On removing sternum there is found interstitial emphysema which extends over upper portion of pharynx and lower portion of neck. Marked hyperemia and edema of all lobes of both lungs posteriorly. Anteriorly, lungs are emphysematous. Larynx, trachea, and primary bronchi contain purulent exudate. Mucosa is slightly roughened, but there is no definite false membrane. There are many small hemorrhages. There is a necrosis of the mucosa of certain bronchi, only in the upper lobes of both lungs. Some of them are lined with a definite grayish-green membrane. There is little fibrinous pleural exudate.

Microscopic examination.—*Trachea:* The epithelium of trachea is completely necrotic and desquamated. Exudate consists principally of pus cells and necrotic material without definite fibrin. Corium is edematous, congested, and infiltrated with leucocytes. Bronchi are similar, but some of them contain an edematous exudate in addition to their other components. Terminal bronchioles are also denuded of epithelium. Many of them are lined with distinct diphtheritic membrane. *Lungs:* Capillaries and alveoli contain an excessive number of polynuclears. There is a granular coagulum in the alveolar spaces and exfoliated, pigment-containing alveolar cells. Polynuclears are not numerous. In Gram-Weigert preparations a wavy, bluish-staining network is seen lying against the alveolar wall in many of the air spaces. Bacteria are not numerous. Predominating type are Gram-positive cocci, arranged in groups. *Kidneys:* There is marked cloudy swelling, especially in the cells of the convoluted tubules. Some tubules contain a pink-staining coagulum, others red blood cells, and still others, desquamated epithelial cells. *Liver:* Capillaries are congested. There is a moderate diffuse fat infiltration. *Adrenals:* Are edematous and congested.

NOTE.—Duration of life after gassing was 5 days. The interesting points in the case are: 1. Very slight cutaneous lesions and apparent absence of ocular lesions. 2. Trachea and large bronchi showed a necrosis and purulent exudate, but no membrane formation. 3. Smaller bronchi were the seat of a typical membranous inflammation, but this was marked only in the upper lobes. 4. Absence of definite pneumonic lesions after five days is unusual. There was, however, a hyaline necrosis of atrial and alveolar epithelium,

which in absence of general lung infection, may be ascribed to the direct action of the gas.

CASE 24.—W. D., 238318, Pvt., Co. I, 103d Inf. Died, 7.30 a. m., October 3, 1918, Base Hospital 15, Autopsy No. 214. Autopsy, October 3, three and one-half hours after death, by Maj. Daniel J. Glomset, M. C.

Clinical data.—Mustard-gas burns and inhalation received in action September 28, 1918. Clinical diagnosis, gas inhalation complicated by lobar pneumonia.

Anatomical diagnosis.—Superficial ulcers of lips; acute conjunctivitis; first-degree burns of scrotum; pseudomembranous and hemorrhagic laryngitis, tracheitis, and bronchitis; peribronchial hemorrhages; confluent lobular pneumonia, left and right upper lobes; hemorrhage into gastric mucosa.

External appearance.—The epidermis about the eyes and conjunctivæ is rough and reddened and covered on the left side by an exudate. Lower lip is swollen and ulcerated. There is a purplish blotch over thorax and abdomen. Skin over penis is swollen, while that over scrotum is swollen and purplish. Blood is laked and black.

Gross findings.—*Pleural cavities:* There are a few fibrous pleural adhesions on the left side, but no fluid. *Lungs:* Do not collapse readily. *Left lung:* Anteriorly is crepitant. Posteriorly it is partially consolidated. On section there are solid areas in lower lobe posteriorly and few discrete nodules anteriorly. These are dark red in color and vary from pinhead in size to several millimeters across and have grayish centers. In one case outside this dark-red area is a slightly raised granular pink zone. In the upper lobe in addition to similar dark areas there is a distinct well-defined consolidation involving one-third of the lobe. *Right lung:* Shows a similar picture. The mucosa of larynx is swollen and roughened. The trachea and bronchi contain greenish thick flocculent material. Mucosa is thick and peels off, leaving a hemorrhagic surface. Bronchi show similar changes. *Heart:* Is normal. *Stomach:* Shows small erosions in the region of the fundus. Small and large intestines are injected. *Kidneys:* Are pale, swollen, and opaque. Remaining viscera seem normal.

Microscopic examination.—The trachea is covered with an exudate, composed of mucus and desquamated and degenerating epithelial cells. There is practically no fibrin and very few leucocytes are present. The epithelium is conserved except at openings of ducts of the glands. It shows striking metaplasia into cells of the squamous-cell type. (See fig. 17.) Submucosa is slightly edematous and vessels are injected. There is very little leucocytic reaction. In the small and medium-sized bronchi the epithelium is partially intact and ciliated. The lumina are filled with purulent exudate. A few of the large bronchi show complete epithelial necrosis with false membrane formation and contain laminated fibrin. The bacteria in the exudate are chiefly Gram-positive diplococci. The blood vessels of the bronchial walls are engorged, and there are hemorrhages in the surrounding alveoli. (See Pl. IX.) The lung shows widespread pneumonic areas. There is an exudate of fibrin and in other places hemorrhage. Leucocytes and red blood cells are well preserved. The process is apparently quite recent. Bacteria are not numerous in the pneumonic patches; in the bronchioles they are quite abundant. There is capillary thrombosis. Interlobular septa are edematous and show an inflammatory infiltration. The unconsolidated portions of the lungs are the seat of patchy nonfibrinous edema, and there is exfoliation of the alveolar epithelium with many of the cells containing pigment. Capillary congestion is marked. *Stomach:* Fresh hemorrhages into the mucosa without necrosis or inflammatory reaction. *Kidneys:* Capsular spaces contain a granular coagulum. There are numerous hyaline casts in Henle's tubules and tubuli recti. *Penis:* The skin over the glans penis is in part denuded. Where it is conserved there is a marked increase in the pigment of the rete mucosum. There is slight papillary edema. Corium contains numerous chromatophores.

NOTE.—Duration of life after gassing was five days. The skin lesions were slight but typical of mustard gas in their character and distribution. The tracheal lesions were slight and regeneration of the epithelium, with the usual metaplasia into the squamous-cell type, had already occurred. Some of the smaller bronchi showed a simple purulent inflammation with intact ciliated epithelium; others showed characteristic diphtheritic necrosis. There were

patches of bronchopneumonia which were not of the influenzal type. On the whole the respiratory lesions were not intense, and in conjunction with the mildness of the cutaneous lesions, imply a short exposure or a low concentration of the gas.

CASE 25.—A. W. G., 2088223, Pvt., Co. A, 355th Inf. Died, August 13, 1918, Base Hospital 116, autopsy No. 12. Autopsy, four hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Mustard-gas inhalation. Date of gassing not recorded. Co. A, 255th Infantry, was exposed to yellow, blue, and green cross shell on August 7 and 8. Autopsy protocols of 9 fatal cases from this gas attack are on file. Admitted in severe condition with burns of face, chest, neck, scrotum, and penis. Temperature and pulse rather high. Respiration short and labored.

Anatomical diagnosis.—Extensive mustard-gas burns of scalp, face, conjunctivæ, neck, buttocks, scrotum, and penis. Acute membranous and ulcerative pharyngitis, laryngitis, esophagitis, tracheitis, and bronchitis. Bronchopneumonia. Marked pulmonary edema. Acute bronchial lymphadenitis. Slight cardiac dilatation. Parenchymatous degeneration of liver and spleen.

External appearance.—The skin has a slight sallow brown appearance. There are extensive superficial burns of the scalp, face, neck, bend of each elbow, the scrotum, penis, the skin of the genital folds and lower buttocks, and in the undersurface of the right knee. There is considerable desquamation of the skin in these areas. There is some brownish pigmentation of the dermis, which is most marked on the inner aspect of both thighs. Superficial glands are somewhat enlarged. Eyelids puffy and glued together by tenacious viscid exudate. The conjunctivæ are edematous and injected. The pupils dilated 5 mm. in diameter. *Ears:* No abnormalities, except the superficial burn of the skin. *Nose:* In the nostrils there is some mucopurulent material. *Mouth:* Shows superficial ulcerated areas of the lips, covered with sordes and viscid exudate. A number of the teeth show gold filling. There is a viscid material over the gums.

Gross findings.—*Pleural cavities:* On opening the thorax, a small amount of fibrinopurulent exudate found free over the pleura of the lower lobe on the right side. On the left there is likewise a small amount of fibrinopurulent exudate, especially marked over the lower portion of the upper and upper portion of the lower lobe. Heart is somewhat enlarged to the right. On incising the pericardium no abnormalities of or in the sac. *Heart:* Weighs 380 grams, the right auricle is moderately dilated. Otherwise normal. *Right lung:* All lobes are voluminous. Upper and middle lobes in great part cushiony, inelastic. In the middle lobe there is a large solid area palpable. Binding the middle lobe to the upper lobe, just above the solid patch there are a number of sheetlike fibrous bands. The pleura shows laterally and posteriorly a considerable amount of fibrinous exudate, below which the pleura is considerably injected and shows numerous small discrete and confluent red hemorrhages. Medially over the upper and middle lobes the pleura is thin and delicate. The glands at the hilum considerably enlarged, pigmented, pulpy, and injected; there is no scarring. Vessels at the hilum show no abnormalities. The bronchi show considerable ulceration of the mucosa; submucosa swollen and injected. Overlying it and the small amount of intact mucosa, there is a cast-like friable gray membrane about 0.5 mm. in thickness. On section of the upper lobe, a moist pink surface presents medially. Posteriorly a pinkish-red surface presents. There is a small amount of thin frothy fluid in the air sacs. Scattered throughout this lobe there are several vaguely outlined dull grayish-red solid patches varying in size from 1 cm. in diameter to several centimeters. The largest patch is present posteriorly. On pressure here viscid fluid exudes from the air spaces. The finer bronchioles are filled with viscid purulent material. The larger bronchial branches show a tenacious fibrinopurulent membrane. The middle lobe on section is in great parts pink and well aerated. There is a small amount of thin frothy fluid in the air sacs. The large solid area is found to be a patch 6 by 4 by 3 cm. uniformly consolidated, dull, and reddish. This portion of the lung is apparently less ventilated than the rest. In the center of the lobe there is a small patch similar in appearance, 1 cm. in diameter. The lower lobe on section presents a moist pinkish-red surface. The air sacs contain a moderate to considerable amount of thin frothy fluid. The bronchial branches show ulceration of the mucosa, with adherent friable gray membrane. About the bronchial branches small and large, there is deep red consolidation

extending for a small distance into the lung. At the periphery of the lung the consolidation about the bronchioles is most marked. *Left lung:* Both lobes are much more voluminous than normal. In the median portion of the lower lobe the tissue is well aerated, euslony; posteriorly, it is soggy. The lower lobe in great part is soggy, and covering the pleura of practically the entire lobe there is a considerable amount of tenacious fibrinous exudate. There is some fibrinous exudate over the lower portion of the upper lobe, especially posteriorly. The glands at the hilum are somewhat enlarged, pulpy, and deeply injected. The vessels and bronchi are similar in appearance to those on the right. On section of the upper lobe it is similar in appearance to the right upper lobe. There is a walnut-sized solid patch posteriorly and a few smaller patches more medially. The lower lobe on section in general is similar in appearance to the right lower lobe, except that here the bronchopneumonic patches are much more numerous and extensive. The edema is most marked in the left lower lobe. *Neck organs:* The glands in the lower portion of the neck are swollen pulpy, edematous injected, and pigmented. In the upper portion of the neck the glands likewise are swollen and injected. The thyroid much larger than normal. Each lobe measures 6.5 by 4 by 3.25 cm. There is a prominent isthmus. On section, the acini are distended with colloid, the tissue gelatinous and pale. In the left lobe there is a hazel-nut sized large cyst filled with gelatinous blood-tinged fluid. The larynx shows marked swelling of the mucosa and deeper tissue. In places the epithelium is gone. In these areas the injection of that tissue below is prominent. Covering the membrane there is a tenacious fibrinous and fibrinopurulent membrane. The process is quite uniform throughout the larynx and trachea and is present likewise in the upper esophagus and the base of the tongue. The tonsils are small and buried. On section there is little lymphoid tissue visible and there is much scarring. In the crypts of the right tonsil there is caked and viscid yellow opaque material. *Alimentary tract:* The stomach, cardiac end, shows moderate patchy injection of the mucosa and there are tiny hemorrhages here and there in this region. *Duodenum:* No abnormalities. Throughout the tract the lymphoid tissue is somewhat more prominent than normal, especially so in the lower ileum. *Appendix:* No abnormalities. *Cecum:* No abnormalities. The mucosa of the colon pale, the walls thinned. Mesenteric lymph glands are slightly enlarged, pulpy, and pale. *Liver:* Weighs 1,800 grams, slight fat infiltration. Remaining organs show no significant lesions.

Microscopic examination—Trachea: Lined with well-formed laminated fibrinous pseudo-membrane invaded with leucocytes and containing in one area in its meshes a large mass of mucus. Beneath the membrane in places is preserved a single row of epithelial cells with pyenotic distorted nuclei, cilia of which are intact. There is marked swelling of membrana propria. Subepithelial tissue, edema, intense congestion, and hemorrhage. Marked leucocytic infiltration. Ducts of the mucous glands are distended with thick plugs of mucus. Epithelium in the superficial portions is destroyed. Additional sections cut from fresh block shows a slightly different picture. Mucosa is partly ulcerated down to perichondrium, the submucosa being in these areas very dense and showing great distortion of nuclei in inflammatory infiltration with pyenotic leucocytes. In other places the epithelium is regenerating, pale, flattened cells covering the denuded surface. These are continuous with the proliferating epithelial cells of the mucous ducts. The sub-epithelial tissue here has the character of very vascular granulation tissue and the predominating cells are lymphoid. There are capillary extravasations and in places much edema. Mucous glands are edematous but the epithelium is preserved. *Lung:* In the terminal bronchioles the epithelium is still present but shows degenerative changes. There is marked leucocytic exudate in the lumina. Consolidation is almost entirely peribronchial. There is a recent pneumonic exudate in which polymorphonuclear cells are predominating. Infundibula are dilated. Another section contains a medium-sized bronchus lined by thickened laminated fibrinopurulent membrane which, together with the looser more purulent exudate, practically occludes the lumen. (Fig. 29.) The epithelium is destroyed and invaded with wandering cells. There is early fibroblastic proliferation. The smaller bronchi on the other hand are free from exudate and show an intact epithelium. Lung tissue itself is emphysematous and atria are dilated. There is practically no pneumonia although there is a little epithelial desquamation and masses of leucocytes in the capillaries. Still another block shows marked dilatation of the atria with some hyaline necrosis of the wall and lobular pneumonia surrounded by areas of patchy edema. Exudate consists chiefly of polymorphonuclears, red blood cells,

and desquamated alveolar epithelium, very little fibrin. There is a purulent bronchiolitis. Gram-positive diplococci, very few Gram-negative bacteria. Remaining organs show no interesting lesions.

Bacteriological report.—Smears of exudate in larynx, Gram stain, show innumerable Gram-positive cocci in pairs and some in small chains. Those in pairs, lancet shape, others rounded. There are also Gram-negative cocci and bacilli. Smears of the consolidated lung show a small number of Gram-positive cocci, most in diplococcus form. No Gram-negative organisms seen. *Cultures:* Trachea, staphylococcus aureus, streptococcus nonhemolyticus.



FIG. 29.—Case 25. Yellow, blue, and green cross shell, exposure 5 or 6 days before death. Dilated bronchiole lined with laminated fibrinopurulent membrane. Complete loss of epithelium

NOTE.—Typical early case of mustard-gas poisoning. There are no precise data given as to exact date of gassing. Since, however, other soldiers of Co. A, 355th Infantry, were gassed on August 7 and 8, 1918, duration of life after gassing may be estimated as 5 or 6 days which corresponds with the anatomical findings.

Points of interest are: The early epithelial regeneration of the trachea, the intense diphtheritic necrosis of the medium sized bronchi, and relatively slight lesions in the bronchioles which seem to have escaped the direct action of the irritant. There was the early lobular pneumonia which presented some of the features of influenzal pneumonia, namely, dilatation and hyaline

neerosis of the atrial walls. There was less hemorrhage and edema and more marked cellular exudation than in the typical case of early influenzal pneumonia.

CASE 26.—I. G., 48449, Pvt., Co. M, 18th Inf. Died, October 6, 1918, 8 p. m., Gas Hospital, Julveecourt. Autopsy, October 7, 20 hours after death, by Capt. James F. Coupal, M. C.

Clinical data.—Gassed with mustard shell on October 1, near Verdun. Diagnosis of mustard-gas poisoning.

Anatomical diagnosis.—Inhalation of mustard gas. Purulent bronchitis and tracheitis. Bronchial pneumonia.

External appearance.—Extensive burns of face, conjunctivæ and cornea. Slight burn serotum.

Gross findings.—*Pleural cavities:* Lungs do not retract on opening the chest. There are a few fresh fibrinous adhesions in the left sac. The right is free. *Right lung* is large. Entire middle, lower, and greater portion of the upper lobes are inflated. There are dark sunken patches along the posterior part of the lower lobe. Firm nodular masses up to 3 or 4 cm. in diameter can be felt through the pleura. Section shows these to consist of areas of peribronchial consolidation. In the center of these areas bronchi appear to be somewhat dilated and filled with pus. The middle lobe shows bronchial lesions, but somewhat less intense than in the remaining lobes. The lower lobe is somewhat edematous, with a few irregular areas of consolidation about the bronchi. *Left lung:* Is very large and heavy, especially about the upper lobe. There is diffuse edema and marked congestion in the posterior portions. The bronchi exude pus and are surrounded by dark-red areas of collapse and hemorrhagic infiltration. The bronchial lymph nodes are dark red, succulent and hyperemic. *Trachea,* as well as the *larynx* and *epiglottis*, show intense congestion and numerous superficial erosions covered in places by shreds of fibrin. This condition becomes more marked in the larger bronchi, where the wall is completely covered by necrotic gray slough. In the smaller branches there is hemorrhagic exudate. *Heart:* Is dilated on the right side. Valves are normal. *Alimentary tract:* Injection of small intestines and stomach; otherwise negative. *Liver, spleen, kidneys:* Show no significant lesions.

Microscopic examination.—*Trachea:* No section preserved. *Bronchi:* The epithelium is desquamated. Lumen filled with pus cells. There is marked peribronchial congestion. *Lungs:* There is general capillary congestion. Alveoli contain polymorphonuclear leucocytes, red blood cells, and edematous fluid and fibrin. The most striking lesion is the marked dilatation of the infundibula with hyaline neerosis of their lining. *Liver and kidneys* negative.

NOTE.—Typical mustard-gas case of five days' duration, with moderately severe tracheal and bronchial lesions. There are no unusual features.

CASE 27.—E. S., 2915502, Pvt., Co. A, 355th Inf. Died, August 13, 1918, Base Hospital No. 46. Autopsy No. 4. Autopsy, 10 hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Gassed on August 8, 1918. Exposed to yellow, blue, and green cross shell. Admitted to Base Hospital No. 46 on August 10 with extensive gas burns of face, neck, trunk, back, and serotum. Severe burns of eyes. Short of breath. Cyanosis. Pulse rapid. Temperature high. Loud moist râles over both chests. Complete aphonia. August 12, slight dullness over both lower lobes posteriorly.

Anatomical diagnosis.—Mustard-gas burns of conjunctivæ, right ear, mouth, chin, genital folds, serotum, and penis. Ulcerative and membranous esophagitis, laryngitis, tracheitis, and bronchitis. Purulent bronchiolitis. Bronchopneumonia. Acute lymphadenitis of bronchial nodes. Pulmonary edema. Gastric and intestinal erosions.

External appearance.—The skin in general is sallow. There are areas of superficial ulceration of the skin about the mouth and chin, back of right ear, in the genital folds, serotum and prepuce. These superficial ulcerated areas extend into the dermis. Those about the mouth are covered with dry scabs; those about the right ear and over the serotum and penis covered by a moderate amount of seropurulent exudate. The eyelids are matted together by a small amount of mucopurulent exudate. The conjunctivæ are edematous, injected. There are small hemorrhages below the bulbar conjunctivæ. The corneæ are slightly cloudy. Pupils 2.5 mm. in diameter. Superficial lymph glands are somewhat enlarged. *Nose:* In the nostrils there is considerable tenacious mucopurulent secretion. The mucosa is injected.

Gross findings.—Pleural cavities: On opening the thorax the right pleural cavity is free of fluid and adhesions. The left pleural cavity contains about 10 c. c. of slightly turbid fluid. The heart lies in normal position. On incising the pericardial sac, no abnormalities of or in the sac. *Heart:* The right auricle and ventricle are slightly dilated. Otherwise normal, except for small grayish flecks in the myocardium. *Right lung:* All lobes are voluminous. The upper lobe is cushiony, inelastic in the upper portion. In the median and lower portion there are solid masses palpable. The middle lobe is cushiony and inelastic. Lower lobe is cushiony and soggy. Near the pleura posteriorly solid masses are palpable. The pleura in general is thin and delicate. Below it, especially posteriorly over the lower lobe, there are scattered and confluent deep red hemorrhages; the small ones pinhead in size and the large ones having an area of a few square centimeters. The glands at the hilum are greatly enlarged, pulpy, edematous, injected, and pigmented; some contain firm gray areas. Vessels at the hilum, no abnormalities. The bronchi show considerable ulceration of the mucosa and covering the ulcerated and intact membrane there is a thin tightly adherent yellowish-gray membrane. Upper lobe on section is pink; in the median portion posteriorly it is red. The bronchi contain fibrinous casts; there is no consolidation about the walls. The air sacs posteriorly contain a considerable amount of thin frothy fluid. The vessels here are somewhat congested. In the median portion there are vaguely outlined dull grayish-red consolidated patches 1 to 2 cm. in diameter. The middle lobe on section presents a very moist red surface. There is a very large amount of thin frothy fluid in the air sacs. Mottling the surface there are large, deep-red, solid, non-air-containing areas varying in size up to 2.5 cm. in diameter. There are larger bronchial branches showing a tenacious fibrinous membrane. The smaller likewise show a fibrinous membrane which in places practically occludes the lumen. At the very periphery of the lobe the bronchi contain a purulent exudate in considerable amount. *Left lung:* Both lobes are much more voluminous than normal. Upper lobe is cushiony, inelastic. The lower lobe is soggy. There are few small solid patches palpable. The pleura is thin and delicate, except posteriorly, where there is some fibrinous and a small amount of fibrinopurulent exudate. Below the pleura here, as on the right side, there are numerous scattered discrete and confluent hemorrhages. The vessels and glands at the hilum similar to those on the right. The bronchi show patchy injection of the mucosa. Everywhere there is considerable tenacious fibrinous exudate. Deep in the smaller bronchial branches there is viscid purulent material in the lumen. The upper lobe on section, a moist red surface presents. The air sacs contain a moderate amount of thin frothy fluid. Posteriorly a few small, solid, non-air-containing, discrete gray consolidated areas observed. Medially there is a small, walnut-sized, solid, dull, pinkish-gray patch. In the lower lobe on section, a deep-red surface presents. The air sacs contain a moderate amount of thin, frothy fluid. Scattered throughout there are deep-red, solid, and non-air-containing solid patches varying in size up to 2.5 cm. in diameter. In addition in this lobe there is some consolidation in the neighborhood of the small bronchioles which are filled with viscid pus. *Neck organs:* Glands in the lower portion of the neck are considerably enlarged, pulpy, and edematous and injected. Some show scarred areas. The glands in the upper portion of the neck moderately enlarged, pulpy, and infected. The thyroid is of average size. On section the tissue is spongy. The acini contain a moderate amount of colloid. *Larynx:* Mucosa is swollen and injected. In places, especially in the region of the true and false vocal cords, the mucosa is ulcerated. The process is similar throughout the trachea, where there are areas of ulceration of the mucosa with injection of the submucosa. Over the intact mucosa and covering the ulcerated portion there is tenacious purulent exudate. The process is present also in the upper portion of the esophagus and base of the tongue, in the region of the glottis. Here, however, there is intense injection of the mucosa and but a few areas of ulceration and fibrinous exudate. The tonsils are buried, scarred, but the crypts are clean. *Alimentary tract:* No other abnormalities of the esophagus. *Stomach:* In the pyloric region shows some 12 or 14 erosions of the mucosa a few millimeters in diameter. In the base of some of these there is a deep-red hemorrhage. Others show a small injected zone about them. The edges somewhat thickened. There is similar eroded area a few millimeters in diameter just beyond the pylorus. The duodenojejunal mucosa is bile stained. *Ileum:* There are scattered patches of injection of the mucosa. The mucosa here, likewise stained with bile. In the lower ileum the lymphoid tissue is somewhat more prominent than normal. There is some injection of the mucosa of the appendix.

There is some patchy injection of the cecum. There is slight diffuse injection of the rectum for a distance of a few centimeters from the anus. The mesenteric lymph glands are slightly enlarged, pulpy, injected. *Liver*: Slight fat infiltration. *Spleen*: Shows moderate lymphoid hyperplasia and hemorrhages into the pulp. *Adrenals*: Show moderate lipid depletion. *Kidneys*: Negative. Remaining organs show no significant lesions.

Microscopic examination.—*Trachea*: Has a well-marked membrane consisting of fibrin, leucocytes, and necrotic cells. The epithelium is lost with the exception of a few squamous cells adherent here and there and a thickened basement membrane. Section of large bronchus also shows epithelial necrosis, the bronchus being lined with necrotic fibrinopurulent exudate which is firmly attached and does not form a loose membrane except in a few places. The wall of the bronchus shows marked inflammatory edema with leucocytic infiltration and intense congestion. Caryorrhexis of the nuclei is very striking. Much chromatin is drawn out into bizarre forms as if melted. *Lungs*: Two blocks of tissue show similar lesions. Very marked edema with little or no fibrin. Alveolar capillaries contain an excess of leucocytes, a few of which have emigrated. There are occasional epithelial cells in the alveoli and scattered hemorrhage. Bronchioles and atria show intact and relatively uninjured epithelium, but contain purulent exudate. There are a few small patches of lobular pneumonia. *Stomach*: Section passes through erosions described in the gross. *Liver, spleen, kidneys* show no significant lesions.

Bacteriological examination.—Smear of exudate from larynx shows Gram-positive and Gram-negative cocci and Gram-negative bacilli. The predominating organism is a Gram-positive coccus in diplococcus form. Smear from consolidated lung shows relatively few organisms. There are Gram-positive diplococci, some lancet shaped, others rounded. No Gram-negative organisms seen. *Culture*: Lung, staphylococcus albus, streptococcus nonhemolyticus. Trachea, streptococcus nonhemolyticus, Gram-positive bacilli.

NOTE.—A very typical early case of mustard-gas poisoning of five days, with necrosis of the tracheal and bronchial epithelium and marked edema. The small bronchioles and atria showed an intact epithelium, although there was a purulent inflammation. There was an early bronchopneumonia. The gastric and duodenal erosions should be noted.

CASE 28.—F. S., 14555, Cpl., 1/4 Highlanders. Died, October 24, 1918, at 6.30 p. m., at Base Hospital No. 2. Autopsy, five hours after death, by Capt. B. F. Weems, M. C.

Clinical data.—October 20, admitted to No. 5, Casualty Clearing Station, with diagnosis of shell-gas poisoning (irritant). October 22, admitted to Base Hospital No. 2. Well nourished; breathes with marked exertion, rapid and fairly deep respirations. Lungs edematous; pale and also somewhat cyanotic. *Heart*: No increase of cardiac dullness beyond normal limits. Pulse 130. Blood pressure 120/85. *Lungs*: Tracheal and bronchial râles; also fine moist râles at both bases. Burn of scrotum. October 23 no improvement in condition. Digitalis and oxygen inhalations; pulse 130, weak and irregular. Chest filled with moisture. October 24, still bravely holding on, but getting tired. Breathing with increasing difficulty. Pale and slightly cyanotic. Becoming very restless. Fully conscious. Anterior chest shows good resonance. Harsh respiratory sound, expiratory sound suppressed. Pulse 140, weak but regular. Died at 6.30 p. m.

Anatomical diagnosis.—Acute conjunctivitis; acute ulcerative pharyngitis; membrano-ulcerative tracheobronchitis; peribronchial adenitis; massive congestion and edema of lungs; ulcerative bronchitis and extensive bronchopneumonia of both lungs; pleural adhesions, right; influenza pneumonia, following inhalation of poisonous irritant gas (?).

External appearance.—Moderate post-mortem lividity. Conjunctivæ markedly injected; corners of the eyes stuck together by dried exudate. Mucopurulent exudate in the nares, nasal mucosa inflamed. No certain evidence of burns upon the skin, but there is one scabbed-over ulceration on the left leg, of uncertain origin. External genitalia are apparently normal.

Gross Findings.—*Pleural cavities*: Lungs meet in almost full inflation. Right pleura free of fluid and adhesions; upon the left side there are soft fibrinous adhesions over a small region beneath the fifth rib in the mammary line and likewise over the dome of the diaphragm. *Pericardial sac*: Contains about 50 c. c. of a slightly turbid, lemon-colored fluid; the membrane

appears quite normal. *Right lung:* Covered over posterior portions by fibrous adhesions. The lung is voluminous, rather heavy, especially in the posterior part; a blotchy gray and purple, very lumpy in consistence. The cut surface is, in general, deep purple, roughly nodular and exudes a large quantity of bloody serum. About the bronchi are grayish red elevated areas of firmer consistence. Upon pressure numerous fine points of pus appear over the surface. The necrosis of the mucous membrane of the bronchi extends into the smallest branches, becoming purulent near the terminal branches. *Left lung:* Early fibrinous pleurisy; quite voluminous; rather firmer in its lower lobe than the right; coarsely nodular throughout. Cut surface presents about the same characteristics as on the right side; there is a rather large area of consolidation in lower portion of upper lobe. Small bronchioles are universally involved and contain either fluid pus or fatty looking plugs of exudate. The edema is exceedingly pronounced. The glands at hilum are acutely inflamed, not frankly suppurative. There is a moderate amount of interstitial emphysema over both lungs. *Organs of the neck:* Pharynx is deeply congested and presents a marked membranous-ulcerative type of inflammation. Tonsils: Are quite small. The inflammatory exudate extends down to the lowest portion of the pharynx. Esophagus: Appears quite normal, but a necrotic membrane extends downward into the glottis. Trachea is filled with a grumous purulent exudate, very foul in odor; the mucous membrane over the vocal cords is entirely sloughed away, and the necrosis extends down the entire trachea into the primary bronchi; beneath the necrotic mucous layer, a roughly granular hemorrhagic surface is revealed. *Heart:* Both ventricles in fair contraction, no lesions. Remaining viscera normal, save for congestion. *Stomach* shows advanced autolysis. Intestines are not recorded.

Microscopic examination.—Pharynx: In some areas the epithelium is still adherent, but dense and shrunken; in other places, the cells show marked vacuolization; in still others, the epithelial cells are vacuolated, but still fairly preserved and probably viable. Where the corium is exposed, it is densely infiltrated with pyenotic leucocytes, and there is fibrin and hemorrhage. The small superficial vessels are thrombosed. Elsewhere, that is in the non-ulcerated areas, there is merely edema with very little inflammatory reaction. The vessels are much congested. The deeper glands are not affected. *Trachea:* No section. *Lungs:* There are extensive patches of pneumonia. The exudate is composed largely of leucocytes which are probably polymorphonuclears, but are remarkable for the fact that the nucleus is displaced to the periphery of the cell, taking a more or less crescentic form. This seems to be due to the ingestion within the cytoplasm of one or more red blood cells and enormous numbers of minute Gram-negative bacilli (*B. influenzae* ?), and lesser numbers of Gram-positive cocci. The same leucocyte not infrequently contains a red blood corpuscle and masses of bacteria. Fibrin is present to a variable extent. The capillaries are engorged with red blood cells, and occasionally contain fibrin thrombi. (See Fig. 20.) There are no larger bronchi in the sections. A medium-sized bronchus shows complete necrosis of the wall, with an adherent fibrin network. The smaller bronchioles contain purulent exudate; and show an epithelial lining which is more or less exfoliated, but not necrotic. Bronchial lymphnodes contain a circumscribed area of fibrinopurulent exudate. *Liver, myocardium, spleen, and pancreas* show no significant changes. *Adrenal* shows marked edema of cortex, with dilatation of cortical capillaries. Areas of focal necrosis (?) in glomerular zone.

Bacteriological report.—Blood culture (post-mortem) sterile.

NOTE.—Presumably an early mustard-gas case, the estimated duration of life after gassing being four to five days. Like a previous case (Case 19), there was slight conjunctivitis, but the cutaneous lesions clinically and at autopsy were insignificant. There was, however, a characteristic diphtheritic necrosis of the upper respiratory passages, in all respects like that of other severe mustard cases. The lung lesions were those of an influenzal pneumonia.

CASE 29.—J. F., 22221, 1/4 Highlanders R. Died, October 25, 1918, at 10.30 a. m., at Base Hospital No. 2. Autopsy, four hours after death, by Capt. B. F. Weems, M. C.

Clinical data.—October 20, admitted to No. 5 Casualty Clearing Station, with diagnosis of shell-gas poisoning (irritant). October 22, admitted to Base Hospital No. 2. Gassed three days ago. Now feels worse. Slight burns of face; eyelids edematous; slight cyanosis; breathes with difficulty; tracheal râles; mucopurulent sputum. *Chest:* Good resonance; coarse and fine râles. Roughened inspiration; expiration markedly reduced. *Heart:* No dilatation ascertainable. Died at 10.30 a. m. Sputum contained pneumococcus, Type III.

Anatomical diagnosis.—Ulceration of upper respiratory passages; acute purulent bronchitis; bronchopneumonia, following inhalation of poisonous irritant gas (?).

External appearance.—Eyelids are edematous and discolored; left ear and left side of face are purple.

Gross findings.—*Pleural cavities:* No fluid or adhesions. The lungs do not collapse and are greatly inflated. *Left lung:* Covered with smooth pleura; larger branches of the bronchi contain thick yellow pus, and their surfaces are in places eroded. On section, droplets of pus exude from each cut bronchiole, and the lung soon collapses markedly. No definite areas of consolidation. *Right lung:* In every way similar to the left, except that there are some small areas of consolidation in the lower lobe. *Organs of neck:* Marked ulceration of the epiglottis and trachea, without a definite membrane. *Heart:* Normal. *Spleen:* Enlarged to about three times normal size. On section, pulp is dark red, moderately firm, follicles small and distinct. Remaining viscera show no noteworthy changes. *Gastrointestinal tract* not described.

Microscopic examination.—*Large bronchi:* The surface is formed by the wavy membrana propria, loosely attached to which are shreds and flakes of very well preserved epithelial cells, in a single flattened row, or in a partly exfoliated layer several cells deep. The cilia are lost, and the cells are partially dissociated by hydropic swelling and leucocytic invasion. The subepithelial tissue is loose and edematous. There is marked congestion and a moderate leucocytic accumulation, chiefly of polymorphonuclears. In the deeper layers the connective tissue cells have the character of fibroblasts and appear to be proliferating. The glands are not affected. There is no membrane or surface exudate. Very few bacteria are present; they are limited to the surface. *Lungs:* There are discrete 2 or 3 cm. sized areas of consolidation between which the parenchyma is relatively normal. These areas are definitely peribronchial. The small bronchioles show a fairly intact ciliated epithelium, but contain a dense purulent exudate with little or no fibrin. The peribronchiolitis shows no special features, apart from the number of large pigment containing alveolar cells. The leucocytes, almost wholly polymorphonuclear, are well preserved. In some of the alveoli are loose masses of cylindrical epithelium, aspirated from the bronchi. Very few bacteria can be demonstrated in Gram-stained sections. *Liver and kidneys:* Show congestion. *Spleen:* Also greatly congested; very few leucocytes in pulp.

NOTE.—A case of poisoning by irritant gas, presumably mustard gas, of five days' duration. There was edema and discoloration about the eyes, but no definite conjunctivitis. The acute ulcerative tracheobronchitis was not membranous in character, and the smaller bronchi showed an acute inflammation, without evidence of chemical injury to the epithelium. The pulmonary lesions were limited to small peribronchial pneumonic areas, and did not have the character of the prevailing influenzal pneumonia. This and the two previous cases (Cases 19 and 28) are peculiar because of the minimal cutaneous lesions. Since the individuals were members of the same organization and were admitted on the same day to the same casualty clearing station, it is very probable that they were exposed to the same gas.

CASE 30.—C. M. S., 134772, Pvt., Battery B, 102d F. A. Died, 1.30 a. m., October 16, 1918, at Base Hospital No. 58. Autopsy No. 5. Autopsy, October 16, 1918, 7 hours after death, by Lieut. H. E. Schoonover, M. C.

Clinical data.—Exposed on night of October 9–10 to bombardment of 2,000 105-mm., and 150-mm. shells of mustard gas and chloropierin. Masks removed prematurely, and soldiers slept in gassed area. Small area attacked, and current kept bringing over the persistent gas. Admitted to Base Hospital No. 58 on October 14. Temperature 103°. Definite signs of lobar pneumonia.

Anatomical diagnosis.—Multiple superficial gas burns. Fibrinopurulent tracheobronchitis. Bronchopneumonia. Emphysema. Chronic fibrinous pleurisy.

External appearances.—Superficial burns over right subclavicular region and both axillary spaces. Rather severe burns about scrotum. Superficial burns on inner aspect of both thighs. Slight burns on both upper eyelids.

Gross findings.—*Pleural cavities:* There are fibrous adhesions at the right apex and over the entire left lung. *Left lung:* There are large extensive subpleural hemorrhages posteriorly

and a little fresh fibrinous exudate. In the upper lobe the bronchi are thick and surrounded by a narrow, sunken red zone. No consolidation. A few small patches of hemorrhagic pneumonia. The smaller bronchi contain pus. *Right lung:* The posterior portion of the upper lobe is congested and edematous. There are ill-defined areas of consolidation. Middle lobe, posterior portion presents the same picture. Lower lobe, extreme base posteriorly shows an area about 3 cm. wide that is definitely consolidated, the cut surface being dark red and granular. The main bronchus to this area shows a moderate diffuse dilatation. Trachea and bronchi show intense congestion and multiple small hemorrhages. Mucosa is opaque and smooth like that of the esophagus and is covered in places by shreds of fibrinous exudate. Mucosa of the bronchi is definitely necrotic and their lumina are filled with exudate.

Microscopic examination.—*Trachea:* On section, shows complete desquamation of the epithelium, which is replaced by thick adherent membrane composed of leucocytes, fibrinous detritus, and masses of Gram-positive organisms. Subepithelial tissue is edematous. The bronchi show no membrane, but the epithelium is necrotic and the lumina are filled with leucocytes. There are many Gram-positive bacteria. *Lungs:* Are slightly edematous with a patchy peribronchial and alveolar exudate of leucocytes with very little fibrin and few red blood cells. The lung lesions, on the whole, are insignificant in the sections examined.

NOTE.—Typical mustard-gas case of six days' duration with early membranous tracheobronchitis and few small areas of lobular pneumonia. There are no features of special interest. Regenerative changes were not present.

CASE 31.—F. J. M., 2280979, Pvt., Co. L, 147th (47th) Inf. Died, August 14, 1918. Base Hospital No. 18. Autopsy No. 79. Autopsy, August 15, 26 hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Gassed August 8, 1918, with mustard-gas shell. Marked erythema over the entire body, particularly marked over chest and about genitals. Marked conjunctivitis, dyspnea, bronchitis, no evidence of consolidation. Frothy, bloody sputum. Burns improved but respiratory symptoms persisted. Pulse rapid and thready.

Anatomical diagnosis.—Extensive burns of respiratory tract, skin, and conjunctivæ. Purulent conjunctivitis. Acute pharyngitis and esophagitis. Acute fibrinopurulent tracheobronchitis. Purulent bronchiolitis. Extensive bronchopneumonia. Pulmonary edema. Acute fibrinous pleurisy. Fatty infiltration of liver. Tuberculous epididymitis.

External appearances.—There is a moderate hypostasis. The skin in general has a muddy sallow-brown appearance. There are in addition scattered areas of deeper brownish pigmentation, especially marked on the inner surface of the thighs, about the knees. The skin shows numerous superficial burns. The burns are most marked in the skin of the back, commencing in the axillæ, extending down the sides, the greater portion of both buttocks being involved. The skin about both shoulders and neck likewise shows superficial ulceration and desquamation. There are large burns on the upper arms, at the bends of both elbows, and on the left forearm. There are scattered superficial burns over the chest and abdomen anteriorly, the skin of the neck and greater portion of the face is desquamated, and in places there are superficial ulcerated areas. The scrotum and penis show superficial ulceration. The base is covered by dry serum. Genital folds show considerable superficial ulceration and desquamation. There are also burns on the under surface of each knee. Above and below the knee on both sides there are areas of clear vesicles, one large bleb. Nowhere does the burn extend deeper than the dermis. Most of the areas are covered by dry serum, below which injected dermis is visible. *Eyes:* Eyelids puffy, matted together by tenacious mucopurulent secretion. The conjunctivæ somewhat injected, and there are small hemorrhages. The corneæ are somewhat cloudy, especially the left. The pupils, 3 mm. in diameter. *Nose:* Tissues puffy. Considerable amount of mucopurulent material in the nostrils. *Ears:* Tissues of the ears are puffy. There are superficial burns about them, covered by desquamated skin and dry serum. *Mouth:* There are superficial ulcerated areas of the lips. The teeth show considerable erosion of the cutting edges. The mucous membrane is cyanotic.

Gross findings.—*Pleural cavities:* The right pleural cavity contains a small amount of fibrinous exudate, lying over the posterior portions of the lower lobe. The left pleural cavity is obliterated in great part by sheetlike fibrous bands. Pericardium normal. On

removing the left lung a small amount of fibrinous exudate is visible over the posterior portion of the lower lobe. *Right lung:* Weighs 1,025 grams. The lower lobe shows a large, deep, congenital fissure dividing it imperfectly in two. The fold is covered by normal pleura. All lobes very voluminous, cushiony, slightly soggy. The pleura over the lower lobe is somewhat glazed posteriorly and laterally, covered by a moderate amount of fibrinous exudate. Below the pleura of all lobes there are scattered small hemorrhages. The vessels at the hilum show no abnormalities. Lymph glands are greatly enlarged, pulpy, edematous, pigmented, injected. Bronchi show considerable ulceration of the mucosa, the underlying submucosa injected. Covering intact and ulcerated mucosa there is a tenacious fibrinous and fibrinopurulent membrane, yellowish in color. On section of the upper lobe a moist pink surface presents medially; posteriorly the surface is a moist red. The air sacs contain a moderate amount of thin frothy fluid. The smaller bronchioles contain a viscid blood-tinged material, the walls are deeply injected, and immediately about the walls the adjoining alveoli are consolidated and deep red. There are a few grayish-red consolidated areas from a few millimeters to $1\frac{1}{2}$ cm. in diameter in the posterior portion of this lobe. The middle lobe on section presents a pink surface. There is a small amount of fluid in the air sacs. The finer bronchioles, similar in appearance to those in the upper lobe, contain fibrinous and purulent exudate. There is but little peribronchial involvement. On section of the lower lobe a moist pink surface mottled with deep red is presented. There is abundant thin, frothy, purulent exudate in places. The walls are injected, the adjoining lung tissue consolidated for a small distance, deep red. In addition there are a number of vaguely outlined, dull, pinkish-gray, consolidated areas, varying in size from a few millimeters to a few centimeters in diameter. These areas are associated with the inflamed bronchioles. *Left lung:* Weighs 1,270 grams. Vessels, glands, and bronchi are similar to those on the right. The pleura over the median portion of the upper lobe is thickened, bound tightly to the parietal pleura by sheetlike fibrous bands. Over the posterior portion of this lobe and the lower lobe the pleura is thin and covered by moderate amount of fibrinous exudate. On section, the left upper lobe is similar to the right upper in appearance. The left lower in general similar to the right lower, but here the consolidation extending from the small bronchioles is much more extensive; reddish gray, involving about one-third of the lobe. In places in the dull, reddish-gray, consolidated portion there are small yellowish areas. *Heart:* There is moderate dilatation of the right auricles and ventricles. Muscle is pale and opaque. *Neck organs:* The lymph glands of the neck and especially those in the lower portion are considerably enlarged, pigmented, pulpy, injected. Thyroid is of average size, tissue spongy, gelatinous. The acini contain a moderate amount of colloid. *Larynx:* There is considerable swelling due to edema of the mucosa; membrane is injected, infiltrated, and covered in places by fibrinous and fibrinopurulent exudate. There are areas of ulceration, especially marked over the true vocal cords. The submucosa is intensely injected throughout lower larynx and trachea. There are small hemorrhages present likewise in this coat. Throughout the lower larynx and trachea there is considerable tightly adherent fibrinous exudate, also a small amount of fibrinopurulent exudate. The injection of the mucosa continues over the glottis into the adjoining esophagus and base of tongue; attached to the injected mucosa in these situations there is a small amount of fibrinous exudate. Tonsils somewhat enlarged, pulpy, and injected. Lymphoid tissue present in moderate amount. There is some scarring. On the left the tonsils show several crypts filled with viscid purulent material. *Liver:* Weighs 2,710 grams. Irregular fat infiltration. *Alimentary tract:* Injected. Stomach and duodenal mucosa injected. Jejunum and ileum edematous. The remaining organs show no significant changes except for the left epididymis, which is thick and on section shows areas of caseation and fibrosis.

Microscopic examination.—Bronchus: There is a complete necrosis of the epithelium, limited in places by the membrana propria, but in other places involving the connective tissue as far down as the glands. There is edema, intense congestion, hemorrhage, and localized collections of polynuclears, all more or less fragmented. The epithelium of the mucous ducts is also completely destroyed. The glands are edematous but still intact. *Small bronchus:* Shows a similar picture except that there is a portion of thick fibrinous membrane still adherent. Masses of bacteria are present on the surface. *Lung:* The bronchioles and atria show complete necrosis of the entire wall; the lumen is filled with detritus and masses of bacteria. The parenchyma throughout shows alveoli filled with

exudate, serous, fibrinous, or hemorrhagic. There are few cells, and these chiefly degenerating and exfoliating epithelium and mononuclears. The relatively few polymuclears show nuclear pyknosis and fragmentation. The alveolar walls are infiltrated with leucocytes, edematous, and often indistinct.

Bacteriological examination.—Smears of trachea show innumerable Gram-positive bacilli and cocci. Smears of consolidated lungs show many Gram-positive lancet-shaped diplococci and rounded Gram-positive cocci. Cultures of tracheal exudate show staphylococcus, nonhemolytic streptococcus, *B. coli* and Gram-positive bacillus. Cultures of consolidated lung show staphylococcus and nonhemolytic streptococcus.

NOTE.—Case of mustard-gas poisoning of six days' duration with typical skin and eye lesions and a severe necrotizing inflammation of the entire upper respiratory tract and extending into the smallest bronchi. The complete destruction of the epithelium would have made repair impossible. The parenchyma of the lung showed a hemorrhagic and fibrinous inflammation like that commonly seen in the influenzal pneumonias. The case illustrates the difficulty in estimating the part played by the original injury and by the supervening infection, respectively.

CASE 32.—R. A., 91283, Pvt., Co. K, 165th Inf. Died, March 28, 1918, 7 a. m., at Base Hospital No. 18. Autopsy, performed nine hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Gassed on March 20 and 21, 1918. On admission, cyanosis, accelerated breathing, irrational. Bronchial fremitus, no signs of consolidation. Dyspnea and polypnea. Pulse rapid and of bad quality. Lungs, hyperresonant and movements limited (inflation). Moist and bubbling râles front and back. At bases are areas of relative impairment.

Anatomical diagnosis.—Superficial burns on eyes, lips, scrotum, and penis. Ulcerative laryngitis, tracheitis, and bronchitis. Bronchopneumonia. Acute fibrinous pleurisy. Obsolete tuberculous bronchial lymph nodes. Healed chronic epididymitis. Fibrosis of myocardium. Dilatation of right ventricle and auricle.

External appearance.—Eyes, bulbar and palpebral conjunctivæ, irregularly injected with small hemorrhages here and there. Gluing the eyelids together is considerable caked exudate. About the eyes a few scabs, especially near the inner canthus on each side. There are similar scabs at the junction of the mucous membrane and skin of the lips. *External genitals:* A portion of the glans penis and greater portion of the scrotum show superficial ulceration, apparently just through the epidermis. The area is dry. In the scrotum at the periphery of the dry area there is an area of moist, very superficial ulceration limited to the epidermis and tissue immediately below. There is a small amount of grayish exudate here and there covering the skin and denuded areas. In the affected parts there is moderate injection of the vessels.

Gross findings.—*Cavities:* On opening the thorax a number of fibrous adhesions are seen between the right middle lobe and chest wall. In the left pleural sac there are a few centimeters of turbid fluid. Heart is displaced slightly to the right. *Right lung:* Weighs 800 grams. All lobes are voluminous. The pleura over the middle lobe is considerably thickened and there are numerous fibrous tags here. Below the pleura in the interlobar region there are numerous discrete pinpoint to pinhead sized hemorrhages. They are present also below the pleura posteriorly. In addition over the posterior portion of the upper and lower lobes there are areas of fibrinous exudate overlying the pleura. The glands at the hilum are strikingly enlarged, pulpy, edematous, and somewhat injected. Some of them contain grayish and yellowish nodules, pinhead to grapeseed in size. On section of the upper and middle lobes a moist pink surface presents. On the section of the lower a moist red surface presents. The bronchial branches are everywhere prominent. They are filled with viscid pus. The mucosa is swollen and injected. In places the mucosa is ulcerated. In all three lobes the air sacs contain a moderate amount of thin fluid, and in places about the finer bronchioles there are small areas of dull grayish-pink consolidation. The consolidation in the lobes on the right is not marked. In most places the consolidation is limited to the area immediately about the bronchial branches. *Left lung:* Weighs 770 grams. All lobes voluminous, soggy in great part. In the lower lobe large solid patches

are palpable. The pleura, especially posteriorly, over both lobes, covered in places by fibrinous exudate. Below the pleura between the lobes there are innumerable pinhead in size hemorrhages. Here, also, there is much fibrinous exudate. Glands at the hilum are similar to the one on the right. On section of the upper lobe a dull pinkish-red surface presents; moist. Air sacs contain a considerable amount of thin, frothy fluid. The bronchial tree throughout filled with viscid pus. The mucosa is injected. The swelling, injection, and ulceration of the bronchial tree is very striking near the roots of both lungs. In the left upper lobe there are scattered small pinkish-gray areas of consolidation associated with the bronchi. In the lower lobe there are scattered throughout a considerable number of grape-seed to hen's-egg sized areas of pinkish-gray consolidation. In addition there is much fluid in the air sacs. *Heart*: Weighs 380 grams. There are small subpericardial hemorrhages. Right ventricle and auricle dilated. Muscle pale with few small scars in left ventricle. Slight chronic aortic valvular disease. *Neck organs*: The larynx and trachea present a striking appearance. The mucosa is swollen, intensely injected, especially in the lower portion of the trachea. There are in places numerous small hemorrhages in this portion. In the lumen there is a considerable amount of viscid mucopurulent material. Tonsils are somewhat buried and small, overlying them there is some desquamation of the epithelium. Tonsils scarred, crypts in general clean. *Liver*: Weighs 2,110 grams. Local areas of fat infiltration. The remaining organs, including the alimentary tract, are normal except for fibrosis of right epididymis.

Microscopic examination.—*Trachea*: There are shreds of epithelium still adherent, but in most places the denuded and swollen membrana propria lies exposed. There is active proliferation of the duct epithelium. In a few places there is necrosis of the superficial portion of the subepithelial connective tissue, which generally is edematous and infiltrated with leucocytes. *Bronchus*: Practically the same picture as the trachea. There is no membrane and the lumen is free from exudate. *Lung*: Two blocks showing similar lesions. The picture is not that of the usual "mustard lung." There is marked and diffuse edema, in places homogeneous, in places distinctly fibrinous. The atria are filled and lined often with a hyaline band. There are dense plugs of exudate in many of the alveoli, the cells differing from normal polynuclears in the shape of their nuclei, which are reniform rather than lobulated. There are many exfoliated epithelial cells, some of which contain pigment, also moderate number of red blood cells. It is hard to make out the walls of the alveoli distinctly. The capillaries are empty, and some appear to contain fibrin thrombi. A small bronchus is filled with pus, but the epithelium is still largely intact. Sections stained with Gram-safranin show innumerable bacteria in the exudate; the predominating organisms are Gram-positive cocci in pairs; and short chains. A few Gram-negative cocci and minute influenza bacillus-like rods are also seen.

Bacteriological examination.—Smears from bronchus show innumerable intracellular and extracellular mouth organisms (Gram-positive diplococci), Gram-negative and positive diplococci, tiny Gram-negative bacilli and diplobacilli. Culture from consolidated lung lost by accident.

NOTE.—Duration of life after gassing, six days. The nature of the gas to which soldier was exposed is not established, but there were characteristic mustard-gas lesions of skin with the usual changes in the trachea and bronchi. There was extensive bronchopneumonia resembling the "influenzal" type. No other special features.

CASE 33.—J. G., 485952, Pvt., Co. B, 47th Inf. Died, 11.30 p. m., October 18, 1918, at Evacuation Hospital No. 7. Autopsy No. 61. Autopsy, October 19, 1918, nine and one-half hours after death, by Capt. James F. Coupal, M. C.

Clinical data.—Gassed on October 12 near Verdun, exposed to blue, green, and yellow cross shells.

Anatomical diagnosis.—Multiple superficial burns. Necrotic inflammation of larynx, pharynx, trachea, and bronchi. Bronchopneumonia (bilateral).

External appearance.—Superficial burns of face, neck, axillæ, hands, scrotum, and conjunctivæ.

Gross findings.—*Pleural cavities*: Left contains many fresh fibrinous adhesions, about 100 c. c. of serosanguineous fluid. The right is obliterated by fresh dense adhesions. *Heart*:

Moderate mitral stenosis. *Left lung*: Is alternately consolidated and congested. Emphysematous along the anterior margins and edematous in dependent portions. The smaller bronchi contain pus. *Right lung*: Same as the left. *Larynx and pharynx*: Markedly injected. Trachea and larger bronchi are denuded of mucosa throughout and are lined with a purulent exudate.

Microscopic examination.—*Trachea*: A few deeply-staining cells are still adherent to the basement membrane. The duct epithelium is also preserved. There is no membrane or exudate on the smooth surface formed by the membrana propria. The subcutaneous tissue is moderately edematous. There is probably a little fibrinous exudate. Very few wandering cells. The congestion of all vessels is marked. *Lung*: (a) Sections show the alveoli lined with coagulum, partly homogeneous, partly hemorrhagic and fibrinous. Leucocytes, mostly polymorphonuclears, are present in variable numbers. Occasional exfoliated alveolar cells are found, but in general they are not distinct. There is marked edema of the interlobular septa, fibrinous and hemorrhagic. No bronchi in section. (b) This block shows a diffuse edema, not intense. A small bronchus is filled with debris of fibrin, fragmenting leucocytes, necrotic epithelial cells. There are fibrin plugs in the adjacent alveoli. In a few places the regenerating epithelium forms a single layer of low cuboidal cells. *Liver*: Central congestion with fatty infiltration and degeneration of cells in center of lobules.

NOTE.—The case illustrates the usual lesion at this stage (six days) following a not too severe injury. There was beginning organization of the tracheal and bronchial epithelium and also the alveolar epithelium in the less damaged regions of the lung. The widespread hemorrhagic edema suggests the prevailing "influenzal" type of infection. The lesions may be ascribed to mustard gas, although there is a history of mixed exposure.

CASE 34.—H. S., 1565196, Pvt., Hdqrs. Co., 18th Inf. Died, October 7, 1918, 3 p. m., Gas Hospital, Julvecourt. Autopsy, two hours after death, by Capt. James F. Coupal, M. C.

Clinical data.—Gassed, October 1, near Verdun. While digging into old gas-shelled hilltop a second gas attack was launched upon the detachment to which the soldier belongs. Nature of gassing not recorded. Clinical diagnosis of mustard-gas poisoning.

Anatomical diagnosis.—Inhalation of mustard gas. Purulent tracheobronchitis. Bronchopneumonia.

External appearance.—Marked burns of face, neck, axillæ, buttock, serotum, upper arms, conjunctivæ, and cornæ.

Gross findings.—*Pleural cavities* normal. *Heart* normal. *Lungs*: Voluminous. Markedly edematous on section with central areas of bronchopneumonia. Bronchi yield plugs of pus. The remaining organs show no significant lesions.

(The following note upon the lesions of the respiratory tract was made at the pathological laboratory, Experimental Gas Field.)

Pharynx normal. The under surface of the *trachea* and *epiglottis* rough and covered with bloody mucus, not definitely ulcerated. *Bronchi* are filled with very abundant blood-stained purulent exudate. No membrane. *Right lung*: Is very fluffy and voluminous, especially the middle lobe, which shows maximum inflation. The pleura is everywhere smooth. On section the upper lobe is dry and air containing. The middle lobe is pale, emphysematous, and dry. Lower lobe is also free from consolidation. No edema. All bronchi exude pus on pressure and show swollen mucous membrane. A small nodular focus of bronchopneumonia about the size of a bean is found on the mesial surface just below the main branch of the pulmonary vein. *Left lung*: Is also large and emphysematous, and there are a few irregular areas of atelectasis which extend a millimeter or so into the lung substance. On section, the lobes are dry, free from edema and consolidation. The bronchi are filled with purulent blood.

Microscopic examination.—The lung is slightly emphysematous in one section. The smaller bronchi are filled with pus cells, there being a general capillary bronchitis. There are a few patchy areas of pneumonia where the groups of alveoli contain polymorphonuclear leucocytes and large cells filled with anthracotic pigment. Capillary vessels are congested.

NOTE.—The case is one of six days' duration. The pulmonary lesions were practically confined to the small bronchi and infundibula, and the emphysema and atelectasis resulting from their partial occlusion. There were typical skin burns, so that the diagnosis of mustard-gas poisoning is unquestioned.

CASE 35.—S. 2108. L/Cpl. 1/Gloucester R. Died, September 24, 1918, at 5.30 p. m., at Base Hospital No. 2. Autopsy, three and one-half hours after death, by Capt. B. F. Weems, M. C.

Clinical data.—September 18 admitted to No. 47 Casualty Clearing Station. Poisoned by shell gas (irritant). September 19 admitted to Base Hospital No. 2. Markedly cyanotic and breathing with much difficulty; profuse mucoid sputum. Burns of lips and nose; congested conjunctivæ. *Lungs:* Moisture generally; pulse, 116; heart, dullness 2 cm. to right of right sternal margin, left to nipple line. Oxygen administered. 1 p. m., pulse 150, marked cyanosis. Venesection 400 c. c. Strophanthin 1/500 gr. intravenously. At 2 p. m., much improved. September 20, doing nicely. Has been getting digitalis. Blood culture sterile. Sputum: Hemolytic streptococci predominating. No tubercle bacilli. September 22, feels much improved; still cyanotic; mucoid sputum. *Heart:* No enlargement. *Lungs:* Marked prolongation of expiratory sounds, few squeaks and coarse râles. September 24, still cyanotic, respiratory difficulty. *Lungs:* No signs of consolidation. Expiration prolonged. Pulse good. 2 p. m., acute attack of severe dyspnea and cyanosis. Pulse rapid and weaker; died at 5.30 p. m.

Anatomical diagnosis.—Acute pharyngitis and laryngitis; intense purulent and ulcerative inflammation of trachea and bronchi; diffuse bronchopneumonia and multiple abscesses of both lungs; pulmonary edema; interstitial emphysema; acute fibrinous pleurisy; old pleural adhesions; healed tuberculosis of right apex; acute suppurative adenitis of peribronchial glands; healed tuberculosis of bronchial glands; congestion of abdominal viscera.

External appearance.—Herpetic eruption on lips (burns?); teeth in very poor condition, many missing, others carious. Dried blood-tinged exudate in the corners of the eyelids, evidence of recent conjunctival inflammation; several small ecchymoses in the bulbar and palpebral conjunctivæ. Dusky cyanosis about ears, cheeks, and posterior part of neck. Mucous membrane over nasal septum much injected; external orifices negative.

Gross findings.—*Pleural cavities:* Lungs are fully inflated and pale. No fluid in pleural sacs. *Left lung:* Exceeding voluminous and does not collapse in the least after severing the bronchus. There are a few fibrous adhesions between the lobes, and several bands near the apex, in which there is a firm calcified nodule. There are a few soft adhesions at the upper portion of the interlobar fissure, which reveals a congested and roughened pleural surface; there is fresh fibrinous exudate along the posterior surface of the lower lobe. The upper and lower branches of the primary bronchus appear very much smaller than usual and are almost entirely occluded by a yellowish-gray, fatty-looking material, and some thinner, almost clear fluid. An occasional bubble of air escapes as the lung slowly collapses. A portion of this occluding material separates readily from the bronchial wall and suggests a fibrino-purulent exudate. A quantity of deep-yellow pus entirely occludes the branches of the bronchi immediately distal. Upon dissection, the mucous membrane of the bronchus appears very considerably thickened, congested at its base, extensively ulcerated superficially, covered by a rather dense, shaggy exudate. Upon section, a striking condition was revealed, bright-yellow points of pus appeared immediately in large numbers, standing out sharply against the bright-red background. There is a deep red areola surrounding each of these purulent points. There are a few small abscesses about the terminal bronchioles. In some areas the inflammation has extended several millimeters about the bronchioles. *Right lung:* Also exceedingly voluminous; heavier in posterior portion than left and has an almost drum-like tightness over the middle and upper lobes, which seem homogeneous and air containing. The lower lobe is firmer, of a peculiar soft doughy consistence. Although there is a great deal of air in the lung, almost no crepitation is felt. The pleural membrane has a glassy appearance and is definitely edematous. Over the lower lobe there is a striking milky opacity of the pleura and a conspicuous edema of the interlobular connective tissue. The superficial blood vessels in the pleura at the base are very much congested; there are a few minute subpleural hemorrhages. The bronchi at the root present a deep congestion with hemorrhages. The glands at the hilum are enlarged and extensively calcified. Upon longitudinal section, a picture similar to that in the left lung is observed. The tissue, however, is somewhat firmer; the surface is more moist and in consistence is firmly nodular. A considerable amount of clear fluid issues from the surface, which has a rather translucent appearance. The general pulmonary inflammation appears more diffuse; otherwise there is little difference from the condition in the left lung. *Heart:* Left ventricle contracted, right rather flabby. No other lesions. *Organs of neck:* The base of the tongue and entire

pharynx are deeply congested and granular. There is a large amount of mucus-pus about the epiglottis and the larynx. The larynx itself and the entire trachea are filled with a foul mucopurulent exudate. The epiglottis is markedly inflamed and covered over its lower portion by a diphtheroid membrane; this extends over the false and true vocal cords, which are congested and swollen. The trachea is inflamed and covered with patches of the whitish membrane. The esophagus is normal. The lymph glands above the bifurcation of the trachea are much enlarged and contain some calcified nodules. *Stomach and duodenum:* Mucous membrane normal. *Intestine:* Not reëxamined. *Other viscera:* No significant changes.

Microscopic examination.—*Trachea:* Patches of necrotic membrane between which the edematous and infiltrated submucosa is covered by a single layer of regenerated epithelial cells, proceeding from the duct epithelium. The new cells are flattened. There is much fibrin and many polymorphonuclears in submucous tissues. Also marked congestion but no hemorrhage. *Large bronchus:* Filled with fibrinopurulent exudate. There is an acute inflammation of the wall which extends to the cartilages. The mucous glands are in hypersecretion. *Lung:* The section includes a medium-sized bronchus entirely filled with purulent exudate, with practically no fibrin. Epithelium is in the form of a single layer of flattened nonciliated cells. Bronchial wall, edematous, hyperemic and infiltrated with leucocytes. There is no peribronchial abscess formation, as was indicated by the gross appearance, but the bronchus is surrounded by a zone of pneumonia in which the exudate is largely fibrinous and beginning to be covered by proliferating alveolar epithelium. In some alveoli there is hemorrhage. Where the pleura is included in the section, it is found to be thickened by edema; the vessels of the deeper tissue are congested. Sections of *myocardium, liver, spleen, adrenals, and pancreas* show nothing interesting.

Bacteriological report.—Blood culture, aerobic and anaerobic media, no growth. Pus from bronchiole: Smear shows a preponderance of short Gram-negative rods, probably *B. influenzae*, also pneumococci and a few streptococci. Culture on agar slant shows only streptococci, which prove to be hemolytic.

NOTE.—Case of six days' duration, probably mustard gas. The burns appear to have been insignificant, being limited to the region of the eyes, lips, and nose. There was a necrotic inflammation of the larynx, trachea, and large bronchi, without the formation of a definite coherent membrane. Epithelial regeneration had begun. There was purulent bronchitis and infundibulitis, with exudate into the surrounding parenchyma, largely fibrinous or hemorrhagic. The alveoli in these peribronchial areas showed beginning epithelial proliferation. Elsewhere there was emphysema and alveolar and interstitial edema.

CASE 36.—E. P. 569343, (?); Sgt., Co. H, 59th Inf. Died, August 14, 1918, at 2.35 p. m., at Base Hospital No. 27. Autopsy, No. 32, performed one and one-half hours after death, by Capt. H. H. Permar, M. C.

Clinical data.—Exposed to mustard-gas shelling on August 8. Extensive skin burns. Gunshot wounds of both feet and left knee; also compound comminuted fracture of first left metatarsal. Admitted to Base Hospital No. 27 on August 12, in a critical condition. Died in delirium.

Summary of gross lesions.—Extensive second-degree burns of face, neck, back, shoulders, arms, and genitals. Left lung weighed 298 grams, right lung 299 grams. All lobes crepitant; no edema or consolidation. Bronchi and trachea negative. Heart muscle flabby; marked dilatation of right ventricle.

Microscopic examination.—*Large bronchus and adjacent lung:* The bronchus is lined with a single row of ciliated epithelium. There is no exudate and the bronchial wall is free from inflammatory changes. The adjoining lung tissue is moderately emphysematous, but not otherwise abnormal. The smallest bronchioles are normal. A medium-sized branch of pulmonary artery shows some adventitial thickening, but is otherwise unchanged. *Lung* (two blocks examined): There is marked emphysema, but no other changes are seen. All bronchioles and infundibula are normal.

NOTE.—Severe and extensive mustard-gas burns of skin, without involvement of the respiratory tract. Death probably due to traumatic injuries six days after exposure to gas.

CASE 37.—J. B., 546888. Cpl., Co. G, 30th Inf. Died, August 16, 1918, at 9 p. m., at Base Hospital No. 27. Autopsy No. 37, performed 28 hours after death, by Capt. H. H. Permar, M. C. (Lieut. F. M. Jacob, M. C.?)

Clinical data.—Exposed to Yellow and Blue Cross shelling on August 10, at Fismes, 75, 77, and 105 mm. shells in attack. Admitted on same day to Field Hospital No. 7 with diagnosis of mustard-gas contact and shrapnel wound of left index finger. August 11 transferred to Evacuation Hospital No. 6. August 12 admitted to Base Hospital No. 27. Severe burns. August 14 crepitant râles and bronchial breathing over both upper lobes. August 15 diffuse crepitant, moist, and bubbling râles at various points over right chest; harsh expiration with loud sibilant rhonchi over lower left lobe. Moderate cyanosis. Bronchial breathing at angle of left scapula. August 16, bronchial breathing over right middle lobe. Breath sounds emphysematous; no signs of edema.

Anatomical diagnosis.—Burns of abdomen, left thigh, and genitals; acute tracheitis and bronchitis, purulent; beginning lobar (?) pneumonia of both upper lobes; emphysema; dilatation of right side of heart.

Microscopic examination.—*Small bronchus:* Purulent exudate fills the lumen. The epithelium is reduced to a few flattened and degenerating cells between the membrana propria and the exudate. There is intense congestion and abundant fresh hemorrhage into the bronchial wall. *Lung:* A medium-sized bronchus shows a partially attached fibrinous membrane. Flattened and highly atypical epithelial cells in a single row are insinuating themselves between the false membrane and the membrana propria. The wall of the bronchus is thick, edematous, and shows fibroblastic proliferation. There is little infiltration with inflammatory cells. The same edematous tissue surrounds the blood vessels. The parenchyma is the seat of confluent lobular pneumonia. The exudate is rich in leucocytes and fibrin. The most striking feature is the regeneration of the alveolar epithelium, the new cells standing out because of their deeper staining. Some of the alveoli show hyaline necrosis. In another section a large bronchus is completely plugged with a fibrinous mass. Attached to this at the periphery are strips of the original epithelium surprisingly little altered. A single layer of flattened cells, many of them degenerated, line the bronchus. The lung tissue shows an extensive fibrinous and hemorrhagic edema very poor in cells. The consolidation produced in this way, though incomplete, is uniform and diffuse. The interlobular lymphatics are distended and contain fibrin clots.

NOTE.—A case of mustard-gas poisoning of six days' duration presenting the usual picture at autopsy. There was beginning epithelial regeneration in bronchi and alveoli.

CASE 38.—C. E. F., 2105082, Pvt., Co. H, 59th Inf. Died, August 15, 1918, 4.45 p. m., at Base Hospital No. 46. Autopsy No. 5, August 15, 11 hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Gassed with mustard gas August 8, receiving severe burns of face, eyes, chest, back, scrotum, penis, and extremities. Unable to talk above a whisper. Eyelids matted together. Foul, purulent discharge from nose. Blood pressure 160/85. Respiration 26, temperature 101, pulse 90, labored respiration. General large moist râles which began on right. Excursion greater on left. Slight flatness over both lower lobes. August 11, diarrhea with bloody involuntary stools, persisting until death.

Anatomical diagnosis.—Extensive burns (gas) of respiratory tract, skin, conjunctivae. Seropurulent conjunctivitis. Acute fibrinous and fibrinopurulent pharyngitis, esophagitis, laryngitis, tracheitis, bronchitis, larynx most marked. Bronchopneumonia both upper lobes. Acute fibrinous pleurisy, left. Acute lymphadenitis regional lymph nodes. Proctitis and colitis, ulcerative. Replacement fibrosis of testes. Cardiac dilatation slight. Pulmonary edema, considerable.

External appearance.—The body is that of a well-built adult male, 168 cm. long. Rigor present to a considerable degree in voluntary muscles. There is considerable hypostasis. The skin in general pale, slightly lemon tinged. There are large areas of ulceration of the epidermis over both buttocks, in the genital fold, backs of both elbows, right shoulder, right upper arm, both forearms, right and left hands. There is considerable ulceration of the epidermis of the scrotum and penis, and there is some matted seropurulent material there. A similar exudate is present over the ulcerated areas of the buttocks and the genital fold;

elsewhere the ulcerated areas are covered by small amount of clotted serum. In the neighborhood of the ulcerated areas there is considerable desquamation of the epidermis. *Eyes:* The eyelids somewhat puffy, conjunctivæ edematous, deeply injected. There are small hemorrhages. Between the lids there is a small amount of caked mucopurulent secretion. *Nose:* Mucous membrane somewhat injected. In the nostrils there is mucopurulent material. *Mouth:* There is some superficial ulceration of the membrane of the lips with slimy material covering the gums. *Teeth:* Show considerable erosion of the cutting edges. *Neck:* Somewhat full in thyroid region. *Chest:* Slightly flattened anteriorly; costal angle about 90°. *Abdomen:* Contour normal.

Gross findings.—On opening thorax, no fluid, no adhesions in right sac. In left sac about 100 c. c. of slightly turbid yellow fluid. Heart enlarged somewhat to right, and on incision no abnormalities, except that there is less fluid present than normal. *Heart:* Normal. *Right lung:* Upper, voluminous; upper portion cushiony; inelastic; lower portion cushiony, soggy, solid. The middle lobe cushiony throughout. The lower lobe cushiony, soggy in addition; small solid patches palpable. Pleura thin and delicate everywhere; below it posteriorly a moderate number of small red hemorrhages. Pulmonary vessels, no abnormalities. Glands greatly enlarged, pulpy, edematous; most of them contain large coherent yellow opaque nodules encapsulated by firm, gray tissue. Bronchi show swelling and intense injection of the mucosa. There is a small amount of fibrinous and fibrinopurulent exudate in places. Upper lobe, on section, upper portion moist, pink; tissue contains a small amount of thin frothy fluid. Section of the lower portion of the lobe shows a very moist, pink and red surface. Air sacs contain a considerable amount of thin frothy fluid. In addition there are good-sized, solid, somewhat granular, dry, nonaerated, deep-red patches, varying in size up to 3 cm. in diameter; associated with these solid areas the bronchioles contain a considerable amount of fibrinous and tenacious fibrinopurulent exudate. These areas are just below the pleura. Middle lobe on section is well aerated. Air sacs contain a small amount of thin, frothy fluid. Lower lobe, on section, tissue in the upper portion pink medially, red posteriorly. There is a moderate amount of thin, frothy fluid in the air sacs. Posteriorly in the upper portion there are numerous deep-red hemorrhages, each several millimeters in diameter. Toward the lower portion of the lobe, the deep-red hemorrhages are more numerous. The tissue contains a moderate amount of thin, frothy fluid. *Left lung:* Both lobes are much more voluminous than normal, especially the upper. Pleura in great part glazed and covered by small amount of tightly adherent fibrinous exudate. The upper lobe cushiony medially, elsewhere soggy. In the mid portion there is an orange-sized, solid, deep-red patch, reaching to and involving the pleura; lower, cushiony soggy. The vessels and bronchi are similar to those in the right. Lymph gland considerably swollen, edematous, injected, and somewhat scarred. On section of the upper lobe, tissue is pinkish red. The air sacs contain a large amount of thin, frothy fluid. In the upper central portion of the lobe there is large, egg-sized, solid, patch relatively dry, granular, and airless. The bronchioles in this lobe toward the periphery show a considerable amount of fibrinous exudate within them. The lower lobe on section similar to the right lower lobe. No distinct, solid, patches; numerous hemorrhages. In this lobe the bronchi show intensely injected, swollen mucosa, with, however, very little exudate. *Neck organs:* The structures of the lower portion of the neck particularly, somewhat edematous. The glands throughout are considerably enlarged, pulpy, injected. Thyroids much smaller than normal. Tissue, spongy and pale. The acini contain but a small amount of colloid. The larynx presents a striking picture; almost completely filling the lumen, there is a large amount of gelatinous fibrinopurulent exudate. The mucous membrane greatly swollen, intensely injected, and covered by tightly adherent, gelatinous, fibrinopurulent exudate. The process is perhaps more marked over the true cords. The mucosa of the trachea is considerably swollen, intensely injected, covered in places by tightly adherent fibrinous and fibrinopurulent exudate. The upper portion of the esophagus and base of tongue show considerable edema of mucous membrane, with scattered patches of injection, in the neighborhood of which there is a moderate amount of tightly adherent, fibrinous, and fibrinopurulent exudate. *Tonsils:* Good size, show considerable amount of lymphoid tissue. There is some injection throughout. *Alimentary tract:* Lower portion of the esophagus, no abnormalities. Stomach shows considerable post-mortem change. Jejunum, ileum, and appendix: No abnormalities. Cecum and ascending colon show considerable diffuse edema of walls, especially of the mucosa. Beginning in the hepatic

flexure and continuing throughout the large intestines and rectum there is marked edema of the mucosa, with innumerable areas of ulceration, about which there is considerable injection, giving the gut a moth-eaten appearance. The ulceration extends into the submucosa. Overlying the ulcerated areas in most places there is an adherent fibrinous and fibrinopurulent exudate in considerable amount. The retroperitoneal and mesenteric glands are considerably enlarged, edematous and pulpy, and injected. The remaining organs show no significant lesions.

Microscopic examination.—*Trachea*: Desquamation of the mucosa; islands of regenerating epithelium still attached here and there. Sections show no membrane or exudate, and no inflammatory infiltration of submucosa, which is intact. *Lungs*: (a) The greater portion of the slide presents the picture of an infected hemorrhagic infarct. There is necrosis of the alveolar walls, blood vessels, and bronchi, with much nuclear fragmentation and scattered colonies of bacteria. The blood cells in some areas are partially decolorized. Thrombi are not found, however. (b) The appearance is that of lung following suffocant-gas inhalation. There is intense alveolar and interstitial edema, partly fibrinous or hemorrhagic, alternating with areas of acute emphysema, in which the dilatation of the bronchioles and infundibula is a striking feature. The epithelium of the bronchioles is perfectly preserved; and there is no pneumonic exudate, although the alveolar capillaries show an increased number of leucocytes. *Large intestine*: Complete necrosis of mucosa, involving the sub-jacent tissue to a variable depth. The superficial vessels are plugged with hyaline and fibrinous thrombi. The deeper layers of the submucosa show an intense hemorrhagic and fibrinous edema, with a moderate lymphoid inflammatory reaction. The muscular coats are not involved. *Testis*: Coarse interstitial fibrosis, with groups of atrophic hyalinized tubules.

Bacteriological description.—*Smears.*—*Trachea*: Innumerable Gram-positive and negative bacilli and cocci. *Lung*: Very few organisms, rounded Gram-positive cocci. *Cultures.*—*Trachea*: *Staphylococcus aureus*, streptococcus nonhemolytic. Gram-positive and negative bacilli (few), aerobic. *Lung*: *Staphylococcus aureus*, streptococcus, Gram-negative bacilli (few), aerobic.

NOTE.—Death occurred seven days after gassing. The history and typical skin burns confirm the diagnosis of mustard-gas poisoning. The lesions of the upper respiratory tract were also typical. The lung lesion, however, differed in some respects from the usual picture. The intense hemorrhage, with infarct-like areas of bacterial necrosis were more like those of the later stages of influenzal pneumonia, although the case occurred at a time when there were few fatal influenzal cases coming to autopsy. Blocks from other portions of the lung showed only an intense edema and congestion, with intact bronchiolar epithelium, and taken by themselves would suggest a diagnosis of phosgene or other gas of the suffocative, rather than irritant or vesicant type. Another interesting feature in the case is the intense hemorrhagic and necrotic colitis, evidently an acute lesion developing after the gassing, and possibly referable to it.

CASE 39.—W. F., 3113960, Pvt., Co. E, 316th Inf. Died, October 16, 1918, 1.45 p. m., at Evacuation Hospital No. 6. Autopsy, October 17, 1918, 20 hours after death, by Capt. James F. Coupal, M. C.

Clinical data.—Mustard-gas burns and inhalation, incurred October 9.

Anatomical diagnosis.—Multiple superficial burns of body. Ulcerative tracheitis (acute). Bronchopneumonia. Acute fibrinous pleurisy.

External appearance.—Marked lividity and diffuse pigmentation over entire body. Burns of cornea, conjunctivæ, face, scalp, penis, scrotum, buttocks, thighs, and knees.

Gross findings.—*Heart* normal. *Pleural cavities*: The left contains 100 c. c. of serosanguineous fluid. Right is negative. *Lungs*: Both are voluminous, alternately consolidated, edematous and congested, and yield, on section, quantities of dark blood and frothy mucus. Emphysema along the anterior margin. *Base of tongue, pharynx, and larynx*: Show beginning ulcerative inflammation extending into whole bronchial tree, with plugs of pus in finer bronchi. *Trachea*: Is denuded of mucosa, which lies in lumen as membrane. *Abdominal viscera*: Congested.

Microscopic examination.—Tracheal epithelium is desquamated to the basement membrane. Here and there a single layer of squamous cells remain. No false membrane is included in the specimen. Corium shows edema, congested capillaries, and round cell infiltration, particularly near the congested capillaries. *Lungs:* Only one block preserved. There is practical occlusion of the small bronchi with dense fibrinopurulent exudate, the epithelium of which shows complete necrosis. There is a zone of fresh hemorrhage about the affected bronchi. Elsewhere no pneumonic exudation or edema except for thready coagulum in a few alveolar spaces. There is a diapedesis of red blood cells throughout the section. *Skin:* Probably of serotum. The stratum corneum is desquamated. Cells in deeper portion of the epidermis are vacuolated. There is a slight edema of the corium. Section taken from skin of eyelid shows similar changes, the edema being more marked. *Cornea:* There is a desquamation of the epithelium of the anterior limiting membrane. Corneal cells and fibrils near the surface are separated, giving a reticulated appearance. *Small intestine, liver, and kidneys* show no significant lesions.

NOTE.—Typical case of mustard-gas poisoning dying on the seventh day after gassing. Although the protocol is not given in great detail and the histological material is inadequate, the case seems to have shown tracheo-bronchitis with membrane formation. The lung lesions appear to be limited to the vicinity of the bronchi, but only one block of tissue was available for study.

CASE 40.—W. B., 1430805, Pvt., Battery B, 102d F. A. Died, October 17, 1918, at 10.30 p. m., at Base Hospital No. 59. Autopsy No. 9. Autopsy, October 18, 11 hours after death, by Capt. M. Flexner, M. C.

Clinical data.—Exposed on night of October 9–10 to bombardment of 2,000 105-mm. and 150-mm. shells of mustard gas and chloropierin. Masks removed prematurely, and soldiers slept in gassed area. Admitted to Evacuation Hospital No. 10 on October 12 with diagnosis of gas inhalation severe, conjunctivitis, serotal burns.

Anatomical diagnosis.—Mustard-gas burns of eyes, nose, mouth, and genitals. Acute fibrinous pleurisy. Emphysema. Bronchopneumonia with miliary abscesses. Membranous and ulcerative tracheobronchitis.

External appearance.—Scabs of mustard-gas burns about eyelids, nares, mouth, and chin. Prepuce and serotum badly burned. No other severe lesions.

Gross findings.—*Pleural cavities:* No fluid. *Right lung:* Shows a fibrinous pleurisy over the lower two-thirds of the upper, the entire middle, and lower lobes. On section there are scattered elevated flesh-colored and reddened areas of consolidation tending to become confluent at the base of the upper lobe. Thick yellow pus exudes from the bronchi and smaller bronchioles. *Left lung:* Also shows fibrinous pleurisy. On section there are similar areas of consolidation, in addition to which at the base of the upper lobe many miliary abscesses, from which a thick yellow pus exudes on pressure. These are from 3 to 6 mm. in diameter. Walls are roughened. Consolidated portions of the lung are dark red in color. The entire *trachea*, from the epiglottis down to the bronchial tubes, as well as the smallest visible branches are reddened and covered to a greater or lesser extent with a fibrinopurulent exudate, which varies in amount very markedly in different bronchi. In the pharynx is a slight redness and delicate white film. Same in the upper portion of larynx. Below the vocal cords is a heavy sealy membrane, white in color, which merges in the trachea into a mucopurulent exudate, which is less adherent. Mucosa is eroded. Peribronchial lymph nodes are swollen and edematous. The remaining organs show no lesions of interest.

Microscopic examination.—*Large bronchus:* Shows the entire bronchial wall edematous, congested and infiltrated with polynuclear leucocytes. Some of the epithelial cells persist or are in various stages of degeneration. *Lungs:* The alveolar capillaries are congested and contain an excess of polynuclears. The contents of the alveoli are a collection of fibrin and granular coagulum, in which there are large pigmented alveolar cells; some of them containing several nuclei, and moderate numbers of polymorphonuclear leucocytes. Pleura is covered with a recent fibrinopurulent exudate. The smaller bronchi are filled with pus. A second section of lung shows definite abscesses, possibly occupying the distended atria and surrounded by compressed alveoli filled with coagulated blood and serum. *Liver:* In some lobules the liver cells about the central veins are atrophic. Protoplasm shows fatty infiltration. A few cells are necrotic. Capillaries in these areas are congested.

NOTE.—The duration of life after gassing was seven days. Although there is a history of exposure to both mustard gas and chloropicrin, the lesions do not differ from those found at this stage in cases exposed to mustard alone. There was no definite membrane formation in the upper respiratory passages, but much necrosis, hemorrhage, and fibrinopurulent exudate. The miliary abscesses in the lungs were probably an extension of the suppurative inflammation of the atria.

CASE 41.—J. T. A., 3106661, Meech., Co. D, 313th Inf. Died, October 18, 1918, 12.15 p. m., Base Hospital No. 15. Autopsy, October, 18, — hours after death, by Maj. Daniel J. Glomset, M. C.

Clinical data.—Gassed with mustard gas October 9 to 10, near Fresnes; 1,000 77-mm. shells used; exposed five and one-half hours; acute conjunctivitis and bronchopneumonia.

Anatomical diagnosis.—First-degree burns of head, neck, and scrotum. Membranous pharyngitis, tracheitis, and bronchitis. Focal pneumonia in left lower lobe, with patchy hemorrhages in both lungs. Marked congestion of abdominal viscera. There is no detailed description of the gross organs available.

Microscopic examination.—*Trachea:* Is lined with stratified epithelium, showing numerous mitoses (See fig. 30). Superficial layer is flattened and devoid of cilia. Subepithelial layer is not edematous and shows no leucocytic infiltration. There is marked congestion. Mucous glands are normal. *Lungs:* Some of the bronchioles are completely filled with loose fibrin plugs, in which are few polynuclears. Epithelium in places is flattened and evidently regenerating; in other places it is destroyed. The bronchial wall is thickened by marked fibroblastic growth. The parenchyma shows a patchy edema, which about the bronchioles is fibrinous and in some places hemorrhagic. There are desquamated pigmented epithelial cells in many of the alveoli. Another section, evidently taken from the "patchy hemorrhages" mentioned in the anatomical diagnosis, shows a very different picture. The alveoli are everywhere filled with a granular coagulum, more or less decolorized, red blood cells, and pycnotic leucocytes in small numbers, exfoliated and degenerating alveolar cells. The capillaries are filled with poorly staining red cells. There are many bacteria. Not only the alveolar epithelial cells but the endothelial and connective tissue cells show degenerative changes, whether from the infection or the direct action of the irritant it is impossible to say. The changes are evidently not post-mortem because of the excellent preservation of the trachea and other portions of the lung. Probably an overwhelming streptococcal infection on the basis of local gas lesions.

NOTE.—After seven days there was a relining of the trachea with epithelium, which was nonciliated. The initial destruction of the epithelium was probably superficial. The lungs showed areas of hemorrhagic pneumonia, in which there was evidently intense infection and damage to the framework of the alveoli. In other areas the lesions were milder in type and regeneration of the alveolar epithelium was in progress. The walls of the small bronchioles were becoming thickened.

CASE 42.—H. B. M., 1786923, Pvt., Co. F, 316th Inf. Died, October 16, 1918, 7.30 p. m., at Base Hospital No. 59. Autopsy No. 8. Autopsy, 10½ hours after death.

Clinical data.—Gassed on October 9, 1918; inhalation and contact. Conjunctivitis. Signs of bronchopneumonia.

Anatomical diagnosis.—Superficial burns about the eyes and scrotum. Extensive hemorrhagic lobular pneumonia with infaret-like areas. Acute membranous tracheobronchitis.

External appearances.—Conjunctivitis with keratitis of both eyes. Burns of lower eyelids. Healing burns about the scrotum. Large amount of reddish-brown fluid escapes from the mouth.

Cross findings.—*Pleural cavities.*—There is no fluid. There are a few adhesions between the visceral and diaphragmatic pleurae of the lower lobe. *Heart:* Right auricle and ventricle dilated and flabby; otherwise normal. *Right lung:* Shows a fine fibrinous deposit confined

to the middle lobe. The lung is purplish or bluish-red in color with localized dark, reddish-black areas in the middle and lower lobe. On section, these are rather friable and firm. Some of them resemble infarcts. The remaining lung tissue exudes blood-tinged, frothy fluid. *Left lung:* Shows an even more intense edema. Otherwise is the same as the right except for older, more pinkish, patches of consolidation in the lower lobe. *Larynx:* In the region of the piriform sinuses shows a grayish necrotic membrane. The mucosa of the trachea is entirely necrotic, replaced by adherent grayish-yellow membrane. The underlying tissue is blotched with hemorrhages. Same condition obtains in larger bronchi. Lumina are filled with large amount of frothy, blood-tinged, purulent material.

Microscopic examination.—*Trachea:* There is a complete epithelial necrosis, involving the duct epithelium as well as that on the surface. There is no regeneration. There are shreds of adherent false membrane containing colonies of bacteria. There is intense filling of blood vessels of submucosa and deeper layers of connective tissue, with capillary hemorrhages. In places there is a beginning sequestration of the edematous and partially necrotic layer from the deeper tissue beneath. Mucous glands are flattened, atrophied, and in some places necrotic. There is very little cellular inflammatory reaction. *Lungs:* In some of the bronchioles, at least, the epithelium is well preserved. In other lumina there is an exudate; in some places serous and in others purulent and more hemorrhagic. Lung parenchyma shows areas in which alveoli are filled with exudate of leucocytes, red blood cells, and well-marked fibrin network, the adjacent regions showing edema or simply hemorrhage. Capillaries and veins are distended with blood. Many of the atria and alveoli are lined with a pink-staining hyaline band, which appears to be partly formed from the swollen basement membrane. Epithelium is not present. In some of the capillaries there are hyaline thrombi, apparently originating from the fused red blood cells. Another striking feature is the pyknosis of the leucocytes in the exudate and the relatively large percentage of mononuclear cells. Gram-safranin stain shows large number of Gram-positive streptococci.

NOTE.—Mustard-gas poisoning of seven days' duration. There was a complete necrosis of the bronchial epithelium involving the ducts of the mucous glands. There were therefore no reparative changes. There was an extensive hemorrhagic lobular pneumonia, more cellular and fibrinous than the usual influenzal type.

CASE 43.—L. K. J., Lieut., 120th Inf. Died, October 26, 1918, at Base Hospital No. 2, at 9 p. m. Autopsy, 13 hours after death, by Capt. B. F. Weems, M. C.

Clinical data.—Exposed on October 19 to blue, green, and yellow cross shells. October 20, admitted to No. 47 Casualty Clearing Station. October 22, admitted to Base Hospital No. 2. Pyrexia of unknown origin in May, 1918. In hospital two months; has been well since. Now suffering from sore eyes, cough, pain in throat and chest; vomiting; has not eaten for three days. *Physical examination:* Well nourished; slight cyanosis; breathing with slight difficulty; eyes congested, lids swollen; nares discharging; pharynx congested. *Heart* normal. *Lungs:* Few bronchial râles, heard generally; fine moist râles at left base; resonance normal. Slight first-degree burns of axilla and thighs. October 24, condition unchanged. Profuse mucopurulent sputum. Fine moist râles at left base, no localized signs of consolidation. Sputum shows *M. catarrhalis* and pneumococcus, not typed. October 25, no improvement in general condition. October 26, much worse this morning. Cyanosis deeper. Respiration rapid, bloody sputum. Dullness marked in left axilla, extending posteriorly to left base. Distant bronchial breathing. Moist râles over both lower lobes. Pulse, 150. Died at 9 p. m.

Anatomical diagnosis.—Acute tracheolaryngitis and hemorrhagic bronchitis; diffuse lobular pneumonia, with marked edema and congestion; acute serous pleurisy; old pleural adhesions; poisoning by irritant gas, nature undetermined.

External appearance.—Quantity of blood is issuing from nostrils and a sanguineous froth from mouth. External genitalia apparently normal. No cutaneous burns. Slight pigmentation and dried exudate about corners of eyelids; conjunctivæ are normal.

Gross findings.—*Pleural cavities:* Right contains about 100 c. c. of blood-tinged fluid, left about the same quantity. There are fibrous adhesions over entire posterior and lateral surfaces of left upper lobe. *Right lung:* Moderately voluminous; grayish-red and purple

color; pleura over middle and greater part of lower lobes shows fresh fibrinous exudate. Bronchi contain a quantity of bloody froth; their mucous membrane is deeply injected and hemorrhagic. Blood vessels and glands at the hilum are normal. The lung has a lumpy consistence; all three lobes contain extensive areas of incomplete consolidation. The cut surface presents a blotchy reddish-gray and purple appearance, with some areas of a deep-reddish brown; the darker areas stand out somewhat from the surface, are of firmer consistence and almost airless. No evidence of infarction is present. *Left lung:* Is moderately voluminous, rather heavy; the upper lobe is covered with fibrous adhesions; the lower lobe presents a mottled appearance, the light-grayish areas being somewhat elevated but not firm, apparently emphysematous. The lower lobe is pretty diffusely consolidated, but contains a small quantity of air throughout and is flabby. The upper lobe on section presents the same characteristics over the lower half; the anterior and upper half are only slightly involved. There is a group of enlarged firmly calcified glands at the hilum. No acute pleurisy. Blood vessels normal. The bronchi display the same injection and diffuse hemorrhagic inflammation with very little exudate. The cut surface of the lung also has the same general appearance as that of the right, a mottled grayish-red and purple and deep red color with diffuse irregular and firmer areas of partial consolidation. There is a large quantity of sanguineous and serous exudate upon the surface. The smaller bronchi are microscopically normal. No exudate or plugs within their lumina are demonstrable. *Organs of neck:* Pharynx is rather deeply congested. Tonsils are small and scarred. Laryngeal surface of epiglottis reveals an acute membranoleucerrative inflammation. There is considerable erosion of mucous membrane over vocal cords and a slight superficial necrosis of the mucous coat along the entire trachea, with a slightly granular looking exudate. A deep fiery injection extends down the trachea, becoming more intense at the bifurcation. Esophagus is normal. Thyroid gland is somewhat enlarged. *Stomach* normal. *Intestines* not recorded. Other viscera show no significant lesions.

Microscopic examination.—*Trachea:* Epithelium defective, save for a few unattached strips in which the cells are not much altered. The somewhat thickened basement membrane lies exposed, uncovered by inflammatory exudate. There is much hyperemia of the corium, with slight diapedesis and a moderate accumulation of wandering cells, principally small mononuclears. The picture is not that of a severe necrotizing inflammation. Very few bacteria are found on the surface, none in the substance of the trachea. *Lung:* The capillaries throughout are filled with well-stained cells, and there are in places profuse alveolar hemorrhages. In addition the alveoli contain a faintly-stained shreddy coagulum, occasional pigment cells and leucocytes, many of which are pycnotic and fragmented. The most interesting feature of the section is the lining of the walls of the alveoli and of the alveolar ducts, with a pink-staining, fibrinoid membrane, representing probably the hyaline necrosis of the alveolar epithelium plus the basement membrane. The remaining blocks of lung show in sections a similar picture, with one exception, in which there is an area resembling a hemorrhagic infarct, with beginning decolorization of the red cells and massive bacterial growth. The alveolar septa in these areas are necrotic. Sections stained with Gram-Weigert-safranin show practically but one type of organism, Gram-positive cocci, occurring in pairs, or more commonly groups, rarely in short chains, rounded and morphologically resembling a staphylococcus. Many of them are intracellular and partially decolorized. They are irregularly distributed, being more abundant where there is a leucocytic reaction, and very sparse or absent in the areas of simple hemorrhagic edema. *Myocardium, liver, spleen, adrenals, thyroid, and pancreas* show no significant changes.

NOTE.—A case dying seven days after a definite history of being exposed to a mixture of irritant and suffocant shell gases. The ocular lesions appear to have been very trifling, and no note was made at the autopsy of the "slight burns of thigh and axilla" recorded in the clinical history. The lesions of the upper respiratory tract were not sufficiently destructive, and their superficial character after seven days argues against exposure to mustard gas. The smaller bronchi showed only hemorrhage. There was widespread congestion, hemorrhage, and edema of the lungs, but no peribronchiolitis of the type so commonly associated with mustard gas. The inflammatory changes were early and appeared to be associated with a staphylococcus, or mixed staphylococcus and streptococcus, infection.

The case is certainly not characteristic of mustard gas, and the lesions are either to be attributed to a mixture of other irritant and asphyxiating gases or to the development of a severe influenzal pneumonia in an individual who had received very light mustard-gas injuries. The case illustrates very well the difficulties in interpretation which may arise.

CASE 44.—H. W. T. L., 88715, Pvt., R. A. F. 3 K. B. S. Died, October 28, 1918, at 4.30 p. m., at Base Hospital No. 2. Autopsy, four and one-half hours after death, by Capt. B. F. Weems, M. C.

Clinical data.—October 21, admitted to No. 47 Casualty Clearing Station. Gassed and wound of right foot. October 22, admitted to Base Hospital No. 2. Generalized inflammation of the bronchi with signs most marked at left base; also many râles at right base. Severe serotal burn. October 26, doing very poorly; right lower lobe practically useless; stifling inspiration sound; short and faint gurgle as expiratory sound. Outlook bad. Left chest filled with coarse and fine râles. Sputum: Direct smear—short Gram-negative bacillus is predominating organism. October 28, much more rattling in chest. Pulse, 120. Died at 5 p. m.

Anatomical diagnosis.—Extensive burns of skin; acute conjunctivitis; acute membranous pharyngitis, laryngitis, and tracheobronchitis; diffuse peribronchiolitis and bronchopneumonia; emphysema; acute fibrinous pleurisy; old pleural adhesions; acute peritracheal and peribronchial adenitis; congestion of abdominal viscera.

External appearance.—The skin has a dusky discoloration and is extensively desquamating; large areas of maceration and peeling of the epidermal layer over abdomen, chest, and thighs. There is much edema and erosion of the skin over the penis and scrotum and a good deal of moist exudate about the groins and inner aspects of the thighs. There is considerable pigmentation of the skin over the neck and face, a dusky purple discoloration about the eyes, the lids of which show some desquamation of the epidermis and rather marked injection and hemorrhagic inflammation of the conjunctivæ. There is bloody dried exudate in the nares; there are extensive erosions over the buttocks and back. Typically adenoid facies.

Gross findings.—*Pleural cavities:* Lungs in full inflation; there is fresh fibrinous pleurisy over a large part of the posterior surface of the right lung and a few chronic adhesions over base. There is a fresh adhesive pleurisy over lower portion of the lung and old adhesions at base. No free fluid in pleural sacs. *Pericardium* normal. *Right lung:* Quite voluminous, rather light, somewhat denser in posterior portion; does not collapse in the least after severing bronchi, and has a peculiar fluffy feel; grayish white in color anteriorly, blotchy red posteriorly. Almost the entire pleural surface is covered by very thin fibrinous exudate and the pleural vessels are injected. The apex and posterior half of the lung is perfectly aerated and soft; the tissue is air-containing throughout and of an almost homogenous consistence. The bronchi display considerable tightly adherent, rather elastic, semimucous exudate, which is purulent and slightly blood-streaked; the membrane is deeply injected and covered by an ulcerating, partly necrotic layer. There is comparatively small content of fluid in the larger bronchi. Blood vessels normal. Lymph nodes are slightly enlarged and acutely inflamed. On cut surface the lung presents a grayish-pink color with deep reddish-brown spots; surface is moderately moist but not in the least bloody; the dark areas are slightly elevated and somewhat firm; they surround small bronchi, which appear to contain small yellowish-gray plugs of exudate. *Left lung:* Presents the same general appearance as right, and is equally voluminous; bronchi contain the same kind of exudate. Upon cut section exactly the same picture is seen. The tissue is everywhere spotted by small dark areas of bronchopneumonia, surrounded by emphysema. *Organs of neck.*—*Pharynx:* Shows an acute ulcerative and membranous inflammation; the arytenoepiglottidean folds are considerably thickened and covered by a yellowish-gray membrane. *Larynx:* Is covered by membrane and froth; its mucous surface is considerably eroded. The upper portion of the trachea is pale in color; the mucous membrane is in a fair state of preservation; the lower half is deeply injected and covered by a patchy necrotic membrane. The peritracheal lymph nodes are somewhat enlarged and considerably congested. *Esophagus:* Normal. *Thyroid* appears normal. *Intestines* not recorded. *Stomach* and *duodenum* normal. *Heart:* Left chamber contracted, right flaccid. Remaining viscera show congestion, but no other significant changes.

Microscopic examination.—No blocks of trachea and large bronchi. *Lungs:* The largest bronchus in the section is lined with normal epithelium showing hypersecretion of mucus. The lumen is filled with blood cells and leucocytes. Several smaller bronchi also contain blood and show an intact epithelial lining. The parenchyma shows very intense congestion, with areas of alveolar hemorrhage and emphysema. There is a little shreddy coagulum in some of the air spaces and a very moderate stasis of leucocytes in the capillaries and the interstices of the septal tissue. Very few have emigrated into the alveolar spaces. Another block shows a large infected thrombus filling a vessel, which is probably a distended artery; the wall, however, is thinned and infiltrated with leucocytes, so that it is difficult to be certain. The center of the thrombus shows suppurative softening and contains large masses of cocci (Gram-positive), which in some places line the necrotic wall of the vessel. The adjoining lung tissue for a distance of several millimeters is profusely infiltrated with hemorrhage. In this hemorrhagic zone are scattered bacterial masses about which the lung tissue is necrotic. A small bronchus included in this area contains a hemorrhagic purulent exudate, but the epithelium is intact. The predominant organisms in the thrombus are: Gram-positive cocci, 1; in tetrads and groups, 2; in chains, probably staphylococci and streptococci. *Myocardium:* In the adventitia of a small artery is a loose collection of leucocytes, chiefly polymorphonuclear. No other lesions noted. *Liver:* Moderate fat infiltration. *Adrenal:* There are some interesting features. The cortical tissue is very edematous, the capillaries of the reticular zone congested. The cortical cells are not vacuolated. Many of them are in various stages of necrosis; others are deeply stained and give the appearance of regenerated cells. This is supported by the finding of numerous mitotic figures, especially in the deeper layers of the fascicularis and reticularis. The chromaffin staining of the medullary tissue is faint or absent in many cells. There are small groups of lymphoid and plasma cells in the medulla. In some areas of the cortex the cells have disappeared, being replaced by the edematous stroma; about the degenerating remains are leucocytes. *Spleen:* Pulp shows hemorrhages, is cellular, and contains a slightly increased number of polymorphonuclear leucocytes. *Kidney:* Intense congestion. In one block there are suppurative foci surrounding bacterial emboli in the pyramidal capillaries. There is hemosiderin deposit in the epithelial cells of the loops of Henle, such as is seen in chronic passive congestion. *Small intestine:* There is hemorrhage into the tips of the villi, with exfoliation (post-mortem ?) of the overlying epithelium. No thrombi, no inflammatory reaction.

Bacteriological report.—Blood culture (post-mortem): Pneumococcus, not typed. Lung culture (post-mortem) on blood agar plate, *B. influenzae* greatly predominates; few hemolytic streptococci, few staphylococcus aureus, few *M. catarrhalis*, Gram-positive and negative bacilli, undetermined.

NOTE.—Mustard-gas case of seven days' duration. The diagnosis is evident from the gross cutaneous lesions and the intense diphtheritic inflammation of the upper respiratory passages. The presence of an infected thrombus in one of the lung arteries and a suppurative lesion in the kidney suggest a generalized bacterial infection; the acute focal myocarditis further supports this view. Although pneumococci were recovered from the heart's blood at autopsy, it is doubtful whether these were responsible for the metastatic lesions. The source of the generalized sepsis is also uncertain. It may have been in the infected wound of the foot, which is recorded in the clinical history, though not described in the autopsy protocol. The lesions in the adrenal cortex are interesting and suggest a severe injury, with early regeneration. The hemorrhages in the intestine may be comparable to those produced by the intravenous injection of dichlorethylsulphide in animals, or they may be associated with the very extensive skin burns.

CASE 45.—J. T., 552741, Pvt., Co. M., 38th Inf. Died, August 15, 1918, at 10.30 a. m. at Base Hospital No. 27. Autopsy No. 33, performed two and one-half hours after death, by Capt. H. H. Permar, M. C.

Clinical data.—Exposed to mustard-gas shelling on August 8. After passing through Field Hospital No. 6 and Evacuation Hospital No. 7, was admitted on August 12 to Base

Hospital No. 27. August 14, diffuse large moist râles, especially on left side. Pulse, 132. August 15, many areas of high-pitched percussion noted; prolonged harsh respiration. Died at 10.30 a. m.

Summary of gross lesions.—Excoriations of skin of face, arms, buttocks, and genitals. *Pleural cavities:* Clear. Both lungs voluminous, weight (of each) 750 grams. Cut section shows marked edema with areas of peribronchial consolidation. The bronchi are filled with fibrinous exudate; there is loose membrane in the larger branches. *Trachea and larynx:* Ulcerated, partially covered with exudate. *Circulatory organs:* Negative. Old tuberculosis of peribronchial glands.

Microscopic examination.—*Trachea:* There is a continuous false membrane. In the areas where this is unattached, a single row of flattened epithelial cells is interposed. The submucosa is edematous but not congested. There is a striking paucity of leucocytes; the few that are present are fragmented and pyknotic. The epithelium of the mucous ducts is in active proliferation. *Medium-sized bronchus:* There is diphtheritic necrosis, with masses of bacteria in the lumen, and here and there early regeneration of epithelium. The outstanding feature is the copious hemorrhage in the walls of the bronchi and the adjacent alveoli. *Lungs:* Bronchioles are filled with plugs of fibrin, in which are masses of bacteria and nuclear detritus. There is profuse alveolar hemorrhage in the neighborhood of the bronchi. In other areas the exudate is rather fibrinous. There are very few leucocytes. Another block shows similar changes in the bronchi and peribronchial tissues. The rest of the lung is markedly emphysematous and anthracotic.

NOTE.—A case of mustard-gas poisoning of seven days' duration. There was the typical diphtheritic necrosis of trachea and bronchi. The pulmonary lesions were chiefly a fibrinous and hemorrhagic edema and appear to have been confined to the vicinity of the bronchi.

CASE 46.—H. S., 310789, Pvt., Co. E, 304th Eng. Died, 7.10 a. m., October 14, 1918, at Base Hospital No. 52. Autopsy six hours after death, by Capt. M. Flexner, M. C.

Clinical data.—Gassed with mustard gas shells October 6. Admitted to Base Hospital No. 52 on October 8. For six days fever, rapid pulse, and respiration. Severe mustard-gas burns over face and upper part of body.

Anatomical diagnosis.—Mustard-gas burns on left side of face, neck, and scalp. Acute tracheobronchitis. Bronchopneumonia. Disseminated tuberculosis, both lungs with cavity formation at both apices. Cloudy swelling of kidney.

External appearances.—Burns over entire left side of face, ear, and neck, extending up to scalp. Scab formation with beginning healing in deeper areas, left ear particularly involved. Burns of first degree with vesicles on right hand. Occasional small vesicles on abdominal wall. No burns of penis or scrotum.

Gross findings.—*Pleural cavities:* There are a few old fibrous adhesions on both sides but no fluid. *Right lung:* At the apex there is a small calcified nodule one-half centimeter in diameter. At the base of the upper lobe is an area 3 to 4 cm. in diameter, grayish purple in color. The remainder of the lobe is mottled pinkish gray. Much fluid can be expressed. Middle lobe is normal. Pleura over the lower lobe is covered with a fine yellow layer of fibrin. Upper pole of the lobe is firm with scattered grayish areas varying in consistency from smooth caseous material to that undergoing purulent degeneration. *Left lung:* The pleural surface is dull. At the apex of the upper lobe is an old dimpled scar 4 cm. in diameter, beneath which on section is a cavity 2 by 3 cm. with fibrous thickened wall. Throughout the entire lower lobe are small calcified nodules. Lung tissue is purplish red in color with scattered irregular yellowish areas 2 to 5 mm. in diameter. A moderate amount of blood-stained fluid. *Trachea* appears red and congested. Peribronchial lymph glands are injected and pigmented. *Heart:* Normal. *Stomach and intestines* are "grossly normal." *Kidneys* show cloudy swelling. Remaining organs present nothing of interest.

Microscopic examination.—*Trachea:* On section, the epithelium is stratified, the lower layer of cells being columnar, the upper layers being polymorphous and generally polygonal. In another section, presumably a main bronchus, epithelium is largely desquamated; it is composed of a single layer of polygonal or columnar cells, very ragged and irregular in their arrangement. Submucous layer is congested, somewhat edematous, and infiltrated with

various mononuclear inflammatory cells, especially about the submucous glands. *Lung:* The parenchyma is the seat of an extensive pneumonic process, showing red cells, leucocytes, fibrin, and large mononuclear cells with pigment, etc. Capillaries are congested. In some areas there are large clumps of bacteria in the alveoli and the surrounding tissue is necrotic. One very extensive area of necrosis is associated with a thrombus in a branch of the pulmonary artery. There is no suggestion of tuberculosis in the three blocks taken. *Skin:* Under the intact epithelial layer there are pigment cells in the corium. Vessels are congested. In another part epithelium is congested and composed of two layers of polymorphous cells with layer of keratin above them.

NOTE.—So far as can be judged from the gross lesions and section, the injury to the upper air passages was slight and repair almost complete. There was an extensive hemorrhagic lobular pneumonia with areas of definite necrosis, in part associated with thrombosis of the vessels. Although from the gross description there were obviously a few obsolete tuberculous lesions at the apex, the histological studies show that there was no disseminated tuberculosis. The occasional areas described might correspond to the areas of definite necrosis. The extensive cutaneous burns confirm the diagnosis of poisoning by mustard gas. The duration of life was eight days.

CASE 47.—R. T., 113314, Pvt., Co. B, 150th M. G. Bat. Died, March 29, 1918, at Base Hospital No. 18. Autopsy No. 52. Autopsy, 21 hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Gassed in front-line trenches, March 21, 1918. Thirty minutes later his eyes became sore; after one hour vomited. At hospital at Luneville developed dry cough. On admission to Base Hospital No. 18 eyes closed, purulent discharge; pharynx much injected. Blisters on face, neck, and legs. Slight general glandular enlargement; harsh breathing and moist general râles. On March 26, signs of consolidation in left chest, dullness, tubular breathing, and râles. March 27, much tenacious sputum. General râles, harsh breathing with dullness, bronchophony, etc., below right scapula. Dyspnea and cyanosis. Temperature, 103; pulse, 120; respiration, 20 to 36.

Anatomical diagnosis.—First-degree mustard-gas burns of conjunctivæ, eyelids, nose, lips, wrists, axillæ, buttocks, penis, scrotum. Membranous laryngitis, esophagitis, pharyngitis, tracheitis, and bronchitis. Purulent bronchiolitis. Bronchopneumonia. Pulmonary edema. Acute lymphadenitis of regional lymph nodes. Cardiac dilatation. Cloudy swelling of liver and spleen.

External appearance.—Cyanosis of face and scalp. There is considerable desquamation of the skin over the buttocks, to a less extent in the neighborhood of the armpits. Also some on the undersurface of both wrists, about both knees, and in both popliteal areas. There is extensive necrosis of the superficial layers of the epidermis with sheetlike shedding of this necrotic skin. Underlying base, quite clean and moist. A similar picture is seen over the central surface of the scrotum and under surface of the penis. There are also superficial burns about the nostrils, lips, and eyes. In these areas necrotic skin is covered by brown scabs. The necrosis extends a small way into both nostrils and a little beyond the line of closure of the lips. Both conjunctivæ considerably injected, and over the left cornea there is a wedge-shaped area of grayish thickening a few millimeters in diameter. The eyelids are somewhat puffy. The pupils about equal, dilated 5 mm. The greater portion of the nasal and buccal mucosa is pale. Teeth and gums in fair condition. Chest, abdomen, and extremities, except for burns, natural looking. Over the buttocks and wrists there are areas of superficial ulceration. The bases clear. In the left lumbar region behind there is an area of superficial ulceration about 2.1 by 1.5 cm. covered by a dense brown-black scab. About this area there is a zone of desquamated superficial epidermis. There is considerable desquamation of the superficial epithelium of the scalp. No definite ulceration, however.

Gross findings.—*Pleural cavities:* On opening thorax pleural cavities show no abnormalities. *Heart:* Is enlarged somewhat to the right. Weighs 400 grams. All chambers, particularly the left ventricle, moderately dilated. Dilatation most marked in the conus. No abnormalities except endocardium of the left ventricle diffusely thicker than normal. The myocardium is boiled in appearance. *Right lung:* Weighs 650 grams; *left lung,* 530 grams. All lobes voluminous and soggy. In addition in the right upper lobe a number of

solid patches of good size are felt. Over one of these the pleura is slightly glazed, glistening everywhere else. The glands at the hilum greatly enlarged, pulpy, edematous, injected. The bronchial tree throughout shows almost complete necrosis of the epithelium. Only here and there are islands of intact mucosa observed. The underlying tissue is intensely injected, and in the smaller branches there are almost occluding fibrinous casts. In places the finer bronchioles contain viscid pus. This picture is present in all lobes. In addition there are scattered areas of whitish-yellow consolidation. In some places these solid patches are associated with atelectatic lung, in others there is no associated atelectasis. The solid areas, varying in size from grape seed to walnut, are most numerous in the right upper lobe. Some are present in the right lower. A few small patches only in the left lower and upper lobes. In addition all lobes contain a moderate to considerable amount of thin frothy fluid in the air sacs. The edema is most marked in the upper lobes. Between the lobes on the right there is a very small amount of fibrinous exudate. Here also there are a few small discrete red hemorrhages below the pleura. There is a moderate number of discrete recent subpleural hemorrhages between the left upper and lower lobes. *Organs of neck:* The anterior mediastinal, tracheal, and cervical glands, especially those in the lower portion of the neck, greatly swollen, edematous, injected. Thyroid, no abnormalities. Acini contain considerable colloid. The trachea and larynx show practically complete necrosis of the epithelium. In places the necrotic epithelium is gone, and in places it is present and readily strips. The underlying tissue intensely injected, especially marked lower down in the trachea. In the lumen there is some fibrinopurulent exudate. In the larynx, affecting the epiglottis and vocal cords true and false, in addition to the necrotic epithelium there is a considerable amount of caked fibrinous exudate. Epithelium and exudate strip fairly readily. The upper portion of the esophagus presents picture similar to that of the larynx. The posterior pharynx, especially about the uvula, similar in appearance. Tonsils are somewhat enlarged, buried, in part, scarred, in part pulpy. Many of the crypts contain viscid or caked purulent and necrotic material. *Alimentary tract:* In addition to the lesions in the upper esophagus there is considerable digestion of the mucosa of the lower portion and of the gastric mucosa. The lymphoid tissue of the tract slightly more prominent than usual. The large intestines considerably distended with gas as far as the splenic flexure. *Adrenals:* There is some diminution of the lipid material in the cortex and in addition the vessels in the deeper layer of the cortex injected. In places there appear to be small hemorrhages. The mesenteric glands are slightly enlarged, pulpy, pale. The remaining organs show no lesions of interest.

Microscopic examination.—Trachea: No preserved epithelium; surface formed by a wavy hyaline band. No exudate or membrane. Submucosa moderately edematous. Loose infiltration of polymorphonuclears, lymphocytes, and plasma cells. Glands show little alteration. Vessels dilated, few capillary hemorrhages. Very few bacteria on surface. *Lungs:* Bronchi present a variable picture. One shows in one place a thick adherent fibrinopurulent membrane, beneath which the epithelium is necrotic. On the opposite wall the bronchus is lined with a single layer of flattened nonciliated epithelium. (Fig. 30.) The picture in the alveoli is a complicated one. There are areas of lobular pneumonia, hemorrhagic in the periphery, which are not especially distinctive. The leucocytes are fragmented. In the unconsolidated areas the alveolar septa are thick and cellular. The cells include relatively few polynuclears, but many large and small mononuclears, plasma cells, and a fair number of eosinophiles. In the alveoli are desquamated epithelial cells, entangled in a fibrinous matrix, over which the regenerated cylindrical epithelium is often growing. In some alveoli are sheets of cells with pale nuclei and indefinite outline, probably actively growing masses of epithelium. Some of the new cells are multinucleated. In other alveoli there is a structureless coagulum incompletely filling the space. A few cocci are present in the pneumonic areas, especially the somewhat dilated infundibuli. Elsewhere they are not found.

Bacteriological examination.—Smears of the bronchus show a large number of Gram-positive and negative diplococci; many tiny Gram-negative bacilli. Smears of the lung show a few Gram-positive diplococci. Cultures from the bronchus show Gram-positive cocci and numerous Gram-negative diplobacilli (influenza). Cultures from the lung show Gram-positive cocci, suggesting pneumococci.

NOTE.—Mustard-gas poisoning of eight days' duration. Typical lesions of skin and respiratory passages. Trachea had been cleaned of exudate.

No epithelial regeneration in section examined. Bronchi showed early regenerative changes along with the remains of the injury and the supervening infection. Lung showed in some areas active bronchopneumonic lesions; in others, as in previous case, epithelium in the alveoli was being restored and the subsidence of the process is shown by the presence of lymphoid and plasma cells in numbers. Eosinophilic polynuclears were also found, with an edema which is apparently not related to the pneumonic infection.



FIG. 30.—Case 47. Mustard-gas burn, 8 days' duration. Longitudinal section of bronchiole, completely occluded by fibrinopurulent exudate. A few shreds of epithelium are still present

CASE 48.—W. G., 3322314, Pvt., Co. C, 109th M. G. Bat. Died, November 8, 1919, 9 p. m., at Base Hospital No. 87. Autopsy, November 9, 13 hours after death, by Lieut. H. H. Robinson, M. C.

Clinical data.—Detachment exposed to 1,000 mustard-gas shells and 400 blue and green cross shells on night of October 31, northeast of Xammes. Went to sleep in headquarters' dugout, 4 a. m., October 31. When he awoke the place was full of gas. Severe pain in eyes and chest; vomiting. Admitted to Base Hospital No. 87 the same day. Increasing bronchitis.

Anatomical diagnosis.—Conjunctivitis. Acute tracheobronchitis. Suppurative bronchiolitis.

External appearance.—No cutaneous lesions. Edema of eyelids with crusts. Slight reddening of scrotum.

Gross findings.—*Trachea:* From epiglottis down, reddened and granular. *Lungs:* Minute foci of consolidation, with small areas of atelectasis and marked emphysema. Lumen of trachea and bronchi filled with greenish pus.

Microscopic examination.—*Bronchi:* The epithelium is intact; there is an albuminous exudate with leucocytes in lumen. Wall inflamed and infiltrated with polynuclear leucocytes. *Lung:* Small patch of beginning bronchopneumonia. Alveoli are air containing. Alveolar capillaries are congested and infiltrated with leucocytes (polynuclear). *Liver and kidney:* Cloudy swelling.

Bacteriological examination.—Staphylococcus and streptococcus in cultures from lung.

NOTE.—Death occurred eight days after gassing. Nature of gas was somewhat uncertain. Conjunctivitis and reddening of scrotum suggest mustard gas, but there were no typical cutaneous lesions and the bronchi did not show the usual diphtheritic necrosis. The material and records of this case are incomplete.

CASE 49.—A. H. P., 2214110, Pvt., Co. G, 4th Inf. Died, August 4, 1918, 12.30 p. m., at Base Hospital No. 46. Autopsy No. 2. Autopsy, August 4, four hours after death, by Capt. Robert Benson, M. C.

Clinical data.—Patient's burns confined to lower extremities and scrotum. Considerable irritative effects of gas could be seen over entire body. Prognosis seemed favorable until 24 hours before death, when patient became delirious and finally toxic. The heart showed the effects of the toxemia and became definitely rapid and weak. Twenty-four hours before death patient had numerous illusions in which he imagined himself in the trenches performing very difficult tasks. At all times he was very restless and complained a great deal of pain about the various parts affected by the gas. Twelve hours before death patient's pulse became almost imperceptible and patient entered a state of coma from which it was almost impossible to arouse him. Restlessness continued until death.

Anatomical diagnosis.—Extensive first and second-degree burns of trunk, extremities and genitalia. Edema and congestion of lungs. Pericardial effusion. Cloudy swelling of liver and kidney.

External appearance.—Surface layers of epidermis denuded and underlying skin of deep red color over greater portion of right arm, upper three-fifths of left arm, greater part of back, nearly whole left flank of trunk, both buttocks, about half of each thigh, greater portion of right leg, portion of left leg, and over penis and scrotum.

Gross findings.—*Pericardial cavity:* Contains 75 c. c. of clear fluid. Both pleural and parietal surfaces show petechiae. *Lungs:* The anterior portion is normal; posteriorly, are dark reddish blue in color with many petechiae. Bloody fluid exudes on section. *Heart* normal. *Alimentary tract* normal except for reddened duodenal mucosa. *Left adrenal,* dark red in color, almost black in places. *Right adrenal,* somewhat enlarged but normal in appearance. *Trachea and bronchi,* apparently were not examined.

Microscopic examination.—*Lungs:* Bronchial epithelium is intact. There is no exudate in the lumen. Alveolar capillaries are tortuous and congested. Slight epithelial congestion and hemorrhage, but no pneumonia. (Two blocks examined.) *Adrenals:* Show excellent preservation. There is no chromaffin staining of the medullary tissue (Zenker's fixation).

NOTE.—No precise data are given as to the date of gassing. Since he was admitted to base hospital on July 27, the duration of life after gassing must have been over eight days.

There are important omissions in the protocol and material for histological examination, since no mention is made of lesions found in the trachea and bronchi, and no sections of these tissues are available. The smaller bronchi showed an intact mucosa and no inflammatory or degenerative changes. The lung tissue itself was congested and edematous, but there was no pneumonia. So far as these findings go, they argue against mustard gas inhalation in lethal

concentration, and this is borne out by the clinical history, which emphasized the mental symptoms, but does not record any respiratory complications. The cause of death in this case is therefore obscure, although the extensive skin lesions with characteristic distribution make it certain that the soldier had been exposed to mustard gas.

CASE 50.—R. P., 2214109, Pvt., Co. —, 4th Inf. Died, August 4, 1918, 10.15 a. m., at Base Hospital No. 46. Autopsy No. 1. Autopsy, August 4, three hours after death, by Capt. Robert Benson, M. C.

Clinical data.—On admission patient was found to have extensive burns over entire back and legs, involving both anterior and posterior surfaces of legs and scrotum. At first patient's appetite was fairly good and he was mentally rational, but patient was seen to be suffering from considerable toxemia. Later as toxemia advanced patient became irrational, stuporous. Temperature remained fairly high; heart action fairly good until 10 hours before death, when it became rapid and irregular. At this time patient became comatose and remained so until death.

Anatomical diagnosis.—First and second degree burns from chemical irritant. Pulmonary edema. Bronchopneumonia, left lower lobe. Pericarditis with effusion.

External appearance.—The skin is denuded over large portion of the body, namely, over left arm from wrist to shoulder, right forearm, whole of left flank, back of trunk. Surface epithelium in these areas is denuded and underlying skin of a deep crimson color. There are a few areas 6 to 8 mm. in diameter in which the deeper tissue is destroyed. Right lower leg and both buttocks are also affected. Skin over penis and scrotum is deep red and swollen but not denuded. Foreskin is greatly swollen but completely covers the glans.

Gross findings.—*Pleural cavities:* Lungs show no adhesions. There is no fluid in the cavities. *Left lung:* Is somewhat firm; over both lobes are areas of annular deep red spots 4 to 8 mm. Cut surface of lower lobe is reddish gray in color and large amount of fluid exudes. The upper lobe is similar but contains more air and is less firm. The pleura, especially in the areas between the lobes, is greenish and edematous. *Right lung:* Lobes on section, are reddish gray and exude a large amount of blood. *Pericardial cavity:* Contains fully 50 c. c. of thin watery fluid. A peculiar pungent odor is observed. *Heart:* Normal. Remaining organs show no significant lesions. *Trachea* apparently was not examined.

Microscopic examination.—*Lung:* Largest bronchus, in section shows practically complete necrosis of epithelium. Membrana propria is swollen and hyaline, resting upon a layer of new formed granulation tissue, infiltrated with polymorphonuclear leucocytes and mononuclear leucocytes. In the lumen is an exudate containing numerous Gram-positive and negative cocci. Other bronchi contain an exudate but show a normal epithelium. Infundibula are somewhat distended and surrounded by areas of lobular pneumonia, with very little fibrin and cellular exudate of predominately polymorphonuclear leucocytes. There is marked congestion and patchy edema. *Liver* shows karyolytic changes in many of the cell nuclei.

NOTE.—A case similar in many respects to the preceding, and since the patient belonged to the same company, was admitted to hospital the same day and died on the same day, the duration of life after gassing was probably the same, namely, over eight days. The skin burns were very extensive, but no mention is made of ocular lesions. The findings in the trachea and bronchi are not given in the protocol and no histological material was preserved. Lung sections showed a bronchiolitis and a peribronchiolitis, the injury to the epithelium varying. Complete necrosis with membrane formation, such as one would expect to find at this stage of mustard-gas poisoning, was nowhere present. These two cases therefore differ somewhat from the usual picture: (1) Clinically, in the marked mental disturbance. (2) In the absence of ocular lesions. (3) In the relatively slight lesions of the lower respiratory tract. It is unfortunate that the records and material are incomplete. It is possible that in these cases the toxemia was comparable to that seen in burns involving

a large part of the body surfaces. It is possible also that the patients were poisoned by some other irritant gas, possibly an arsene compound, and that the divergence from the usual picture is due to this. No evidence is at hand to decide the question.

CASE 51.—J. M., 2181256, Corpl., Co. A, 355th Eng. Died, August 16, 1918, Base Hospital No. 116. Autopsy No. 16. Autopsy, 10 hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Mustard-gas inhalation and contact, incurred August 8, 1918. First degree burns of face, neck, scrotum, penis, and conjunctivæ. On August 12, auricular fibrillations; coarse râles on both sides; labored respiration. August 14, restless and delirious. Last three days signs of bronchopneumonia; purulent sputum; pus and blood from nostrils; edema of face and eyelids.

Anatomical diagnosis.—Gas burns of skin, conjunctivæ, lips. Acute fibrinous pharyngitis, esophagitis, laryngitis, tracheitis, and bronchitis. Acute peribronchitis. Bronchopneumonia. Pulmonary edema. Serofibrinous pleurisy. Acute fibrinous pericarditis.

External appearance.—Skin in general has a slightly bluish tinge, backs of hands, face to a slightly less extent, thighs and upper legs show a diffuse brownish pigmentation. Superficial areas of ulceration of epidermis of genital folds of scrotum and penis, about both lips, right nostril, over left eye, and under surface of both knees, where there is desquamation of the skin with apparently new epidermis below. There is considerable caked desquamation of the scalp, about the ears, chin, and also in the region of the superficial ulcerated areas mentioned above. Along the inner aspect of both thighs, at some distance from the ulcerated areas, there are numerous pinpoint to pinhead sized vesicles. Eyelids are edematous; there is a moderate amount of mucopurulent exudate between the lids. Conjunctivæ are injected with small dark-red hemorrhages. Moderate amount of mucopurulent exudate in nostrils.

Gross findings.—*Thorax:* Left pleural cavity contains 700 c. c. of slightly turbid yellow fluid in which are flecks of fibrinous exudate suspended. Pleural and pericardial adhesions on both sides. *Pericardium:* Both visceral and parietal layers swollen, diffusely injected, and covered by moderate amount of fibrinous exudate, binding the two layers together. *Heart:* Right side is dilated. Myocardium is opaque and flabby. *Lungs:* Right upper and lower lobes are much more voluminous than normal, cushiony, and soggy. In the lower lobe solid patches are palpable. The middle lobe more voluminous than normal, cushiony, slightly soggy. The lower lobe shows a congenital fissure 7 cm. long from the interlobar septum. Pleura posteriorly and between the lobes shows a small amount of fibrinous exudate. The glands at the hilum moderately enlarged, pulpy, edematous, injected, pigmented, show in places old scars. *Bronchi:* Mucosa is moderately swollen and intensely injected, covered in places by fibrinous and fibrinopurulent exudate. There is mucopurulent exudate and thin frothy blood-tinged fluid. On section, upper lobe, a moist pink surface presents. The air sacs contain a moderate amount of thin frothy fluid. The smaller bronchial branches contain a considerable amount of fibrinous and fibrinopurulent exudate, friable in places, and practically occluding the lumen. The walls of these small bronchioles show considerable injection, and the lung tissue about them likewise deeply injected for a small distance. In places in this lobe there is a small amount of peribronchial consolidation. The middle lobe on section presents a mottled pink and red surface. The air sacs contain a small amount of thin frothy fluid. The bronchi are similar to those in upper lobe in appearance. The changes, however, are not quite so marked. In the median portion there is an area of atelectasis. Lower lobe on section presents a mottled pinkish red and reddish purple surface. The bronchial changes are similar to those described above. About the bronchial branches there is considerable injection of the tissue, and toward the periphery there are numerous extensive areas of dull reddish-gray consolidation. *Left lung:* Upper lobe is much more voluminous than normal. Lower lobe somewhat collapsed. The vessels, glands, and bronchi similar in appearance to those on the right. On section of the upper lobe a pink and red surface presents. The air sacs contain a moderate amount of thin frothy fluid. The picture is quite similar to that of the right upper lobe. In this lobe, however, there are a few consolidated patches toward the periphery. The cut section passes through a large pulpy injected lymph gland with numerous soft and firm yellow opaque nodules, varying in size from less than a pinhead to a grape seed.

The consolidation in this lobe is more marked in the lower portion. On section of the lower lobe the tissue is rubbery in consistency, poorly aerated, deep red. Bronchial tree shows a picture similar in general to those elsewhere. The pleura everywhere is glazed and covered by a large amount of fibrinous exudate. On stripping this exudate in places numerous injected vessels can be seen in the pleura. *Neck organs:* Glands through neck considerably enlarged, pulpy, edematous, deeply injected, especially those in the lower portion. *Thyroid:* Of good size, spongy, and gelatinous. There is a moderate amount of colloid in the acini. *Larynx:* There is marked swelling and injection of the mucosa, with small areas of ulceration, especially about the true vocal cords. Within and adherent to the mucosa there is considerable amount of fibrinous and fibrinopurulent exudate. In the trachea the change is less marked. The mucosa is swollen, intensely injected. There are scattered small flecks of yellow opaque exudate. In the lumen there is much mucopurulent and some thin frothy blood-tinged fluid. The posterior pharyngeal wall and upper esophagus adjoining the glottis shows considerable edema and injection of the mucosa; covering the mucosa in several places there is a moderate amount of adherent fibrinous and a small amount of fibrinopurulent exudate. *Tonsils:* Right tonsil not removed. Left tonsil somewhat swollen. On section considerable pulpy, edematous, injected, lymphatic tissue present. Crypts, clean. *Alimentary tract:* No abnormalities of esophagus other than those mentioned above. Stomach contains a small amount of mucus. The mucosa in the fundus is somewhat swollen. The duodenum, the jejunum, and the ileum, no abnormalities, except that the lymphoid tissue is more prominent than normal. Appendix, cecum, colon, rectum, no abnormalities. The remaining viscera show no significant lesions.

Microscopic examination.—*Trachea and large bronchi:* No material preserved. *Lung:* (Block A) Picture is that of late lobar pneumonia. Alveoli are filled with exudate in which there are many fragmented leucocytes and fibrin. Capillaries are thin, collapsed, and empty. Some alveoli are being relined with irregular syncytial growth of epithelium, amongst which are large cells with pale nuclei. (Block B) Intense hemorrhagic edema and epithelial desquamation. Bronchi are distended with solid plugs of exudate. Epithelium completely necrotic. (Block C) Smaller bronchi are the seat of an intense necrosis, often with fibrinous membrane formation. Peribronchial exudate with much fibroblastic activity, especially in the thickened septa. Alveoli contain an exudate which in places is fibrinous, in others hemorrhagic, and others serous. There is not much epithelial proliferation. Atria are filled with purulent plugs. There is an edema of the interlobular septa. (Block D) Evidently taken from the left collapsed lobe, showing usual picture of atelectasis. It is interesting that the bronchi in section show very slight changes, their epithelium being preserved and their lumina free from exudate. *Myocardium:* Recent acute fibrinous pericarditis. *Liver, spleen, and kidneys* normal.

Bacteriological examination.—Smears from exudate on right side of larynx show innumerable Gram-positive and Gram-negative cocci. Smear from consolidated lung show few Gram-positive cocci, most in diplococcus formation.

NOTE.—Typical mustard-gas case, of eight days' duration, with multiple skin burns and diphtheritic necrosis of the larynx, trachea, and bronchi. There was complicating serofibrinous pleurisy and pericarditis. It is worthy of note that the bronchial lesions in the atelectatic lobe were less severe than elsewhere. The focal areas of pneumonia were not of the influenzal type.

CASE 52.—P. B., 113251, Pvt., Co. B, 150th M. G. Bat. Died, March 29, 1918, at Base Hospital No. 18. Autopsy No. 53. Autopsy, 20 hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Gassed on March 21, 1918. On same day, smarting of eyes, burning and blistering of scrotum, and following morning vomiting. Night of 22d, pain in chest and coughing. On admission, severe conjunctivitis. First degree burns of buttocks, thighs, and legs 5 cm. below knee. Anteriorly from patella up to scrotum and perineum. Severe burns of hands and fingers and forearms. March 28, burns healing nicely, but patient appears intoxicated. Acetonuria, March 29, semidelirious.

Anatomical diagnosis.—Second-degree mustard-gas burns of skin over thighs, buttocks, hands. Conjunctivitis. Acute pharyngitis, esophagitis, laryngitis, tracheitis, and bronchitis. Bronchopneumonia. Marked pulmonary edema.

External appearance.—There is considerable hypostasis, with cyanosis of the face and extremities. From the level of the symphysis downward anteriorly and posteriorly the greater portion of the skin of the thighs shows almost sheetlike necrosis, desquamation, and ulceration, which extends in places a small way into the subcutaneous tissue. The base shows patchy injection, and especially toward the genital fold there is a moderate amount of moist, foul-smelling exudate. The penis and the scrotum show necrosis of the epithelium with superficial ulceration. There are well-marked areas of ulceration over both buttocks. The burn continues down and involves the popliteal area. The most extensive ulceration is present over the backs of the hands and undersurface of the wrists, where the subcutaneous tissue is involved. The epithelium over the dorsal surface of the wrists, hands, and to a less extent left forearm is gone entirely. The base of the denuded tissue shows considerable injection. There is a moderate amount of exudate over the wrists. On the left the base is quite dry, brown. There is some desquamation and superficial ulceration of the left forearm. No involvement in the axillæ. Slight involvement of the eyes, especially the left. Conjunctivæ on this side moderately injected. Corneæ show slight milky thickening. There is a small burn at the left angle of the mouth. There is some desquamation of the epidermis over the abdomen, but no ulceration. Left leg and left foot show few areas of necrosis of the epidermis without ulceration, however. *Nose:* The mucosa is somewhat swollen, slightly injected. *Mouth:* There is superficial ulceration of the lips along the line of closure. The buccal mucosa beyond, however, pale, apparently uninvolved. Gums in fair condition. A number of teeth poorly formed.

Gross findings.—*Both pleural cavities:* Free from adhesions. Each contains a few centimeters of fluid. The heart is enlarged somewhat to the right. *Heart:* The right auricle and ventricle moderately dilated. Myocardium is boiled, slightly greasy. No valvular lesions. *Right lung* weighs 655 grams. Pleura thin and glistening in great part. Over the posterior portion of the left lower lobe, however, it is dull gray, and there is a very small amount of fibrinous exudate. Below the pleura, especially posteriorly, there are innumerable discrete and in places confluent hemorrhages varying in size from one to several millimeters. All lobes are quite voluminous, especially both lowers and the posterior portion of the uppers. These areas are soggy in great part. Glands at the hilum are moderately enlarged, pulpy, edematous, injected. The bronchial tree toward the hilum shows considerable diffuse injection of the mucosa without outspoken ulceration. In the lumen there is some frothy blood-tinged fluid and some mucopurulent material. In the smaller bronchial branches, especially in the posterior portion of both lower lobes, there is a fibrinopurulent exudate present, and in the posterior portion of both upper lobes to a less extent. In the upper lobes there are numerous patches of consolidation, deep red, dry, granular, varying in size from pinhead to walnut. In addition both lower lobes and the posterior portion of both uppers show a large amount of thin, frothy fluid in the air sacs. The right middle lobe is relatively uninvolved. The cut surface is pink. *Organs of neck:* The mediastinal and tracheal glands are moderately enlarged, pulpy, and edematous. *Thyroid:* Of average size, pale. Acini contain a moderate amount of colloid. The neck organs present a striking picture. There is moderate necrosis of the epithelium of the posterior pharynx, upper portion of the esophagus, larynx, and upper portion of the trachea. Associated with the necrosis there is a membranous exudate having a necrotic greenish appearance. Throughout the larynx and trachea there is considerable injection and swelling of the mucosa with no ulceration. In the ulcerated area the base is well in the mucosa. Tonsils fair size, buried, in part scarred. The crypts in general are clean. *Alimentary tract:* There is pigmentation of the solitary follicles and Peyer's patches. No ulceration or hemorrhage. *Liver* enlarged and fatty. Remaining organs show no significant lesions.

Micrascope examination.—*Trachea:* Epithelium is lost and no pseudomembrane is present. Submucous layers are congested, edematous, and infiltrated with round cells. *Lungs:* Parenchyma is very much congested. There are areas where the alveoli are filled with red blood cells, and the alveolar walls are necrotic. There is no inflammatory exudate. Bronchial epithelium is preserved. No exudate in the lumina. *Liver and kidneys* show parenchymatous degeneration.

Bacteriological examination.—Smears of exudate from the trachea show innumerable mouth organisms. Smears of the exudate from the lung show large numbers of Gram-positive diplococci, lancet-shaped. Culture of exudate from trachea shows Gram-positive diplococci and tiny Gram-negative influenza bacilli.

NOTE.—Duration of life after gassing was eight days. Lesions of the respiratory tract were not typical of mustard-gas inhalation. Absence of

necrosis in trachea and large bronchi, and simple congestion and hemorrhagic edema of lungs without inflammatory changes did not conform to the usual pictures. Histological material was inadequate, but the clinical and gross findings were sufficiently characteristic to justify a diagnosis of mustard-gas poisoning. The marked post-mortem changes in the adrenal and kidney, and other organs made the interpretation of the findings in these organs difficult.

CASE 53.—L. P. G., 91249, Pvt., Co. K, 165th Inf. Died, March 29, 1918, at Base Hospital No. 18. Autopsy No. 50. Autopsy, four hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Gassed on March 20 and 21. On admission severe conjunctivitis (blindness). Many small blisters on wrists and hands. Forehead hyperemic. Superficial burn of scrotum and inner aspect of thighs. Generalized coarse râles. March 25, eyes better. Temperature elevated. Increased râles, cyanosis. March 27 and 28, bloody sputum, broncho-vesicular respiration left axilla, dyspnea, and increasing râles.

Anatomical diagnosis.—Mustard gas burns of conjunctivæ and scrotum. Fibrinous and fibrinopurulent esophagitis, laryngitis, tracheitis, and bronchitis. Purulent bronchiolitis. Extensive bronchopneumonia. Acute fibrinous pleurisy. Pulmonary edema.

External appearance.—There is considerable hypostasis; marked cyanosis of left side of face and scalp, less marked in lips and right side of face. Over the proximal portion of the upper and lower extremities, especially in the folds, there is much scaling of the epidermis and numerous groups of pinpoint to pinhead sized vesicles, filled with transparent fluid. This condition is present also over the upper and lower back and is most marked on the backs of the hands, scrotum, and penis, where there are outspoken first-degree burns. There are several superficial ulcerated areas covered by scabs about the lips. Superficial glands are palpable. *Eyes:* The right pupil is larger than the left, 4.5 mm.; left, 3 mm. Bulbar and palpebral conjunctivæ somewhat swollen, show extensive patchy injection, and on the left side particularly there are good-sized deep red hemorrhages below the conjunctivæ. The lids are somewhat puffy and glued together by caked exudate. *Nose:* Both nostrils contain clotted blood. Mucosa not appreciably swollen, but pale. *Mouth:* Teeth in fair condition. Gums quite clean. Buccal mucous membrane pale, apparently uninvolved.

Gross findings.—*Pleural cavities:* A few cubic centimeters of fluid in each pleural sac. No fibrous adhesions. Heart enlarged somewhat to the right. *Heart:* Weighs 375 grams. The heart is somewhat enlarged. The tricuspid and pulmonary rings moderately stretched. The conus is greatly dilated. Left ventricle moderately dilated. Valvular endocardium, no abnormalities. Chambers contain large elastic clots. *Lungs:* Right, weighs 630 grams. Left, weighs 475 grams. All lobes are moderately voluminous. Upper and middle lobes cushiony, somewhat soggy. The lower lobes soggy and solid. Covering both lower lobes posteriorly there is a moderate amount of fibrinous exudate. In these regions and also in the interlobar areas there are numerous subpleural pinhead sized red hemorrhages. Glands at the hilus on each side greatly enlarged, pulpy, edematous, moderately injected, some areas show scarring. The bronchial tree throughout presents a striking picture. There is practically complete desquamation of the epithelium. The submucosa is apparently injected and covered by a layer of friable to elastic coherent light whitish-yellow exudate, in the larger bronchi over 1 mm. in thickness. These fibrinous masses form a large cast of the bronchi and are readily stripped from the walls. The process is most marked in the lower lobes, is present also in the right upper and middle, and less marked in the left upper lobe. In the finer bronchioles of all lobes, but most marked in both lowers and the right upper, the exudate is viscid purulent, rather than fibrinous. Associated with some of these areas of purulent bronchitis there are patches of grayish red consolidation of the lungs. These areas of consolidation are most numerous in the lower lobes, perhaps more numerous in the left than the right, and here they vary considerably in size up to large walnuts. In addition all lobes, especially the lower, show a moderate amount of thin frothy fluid in the air sacs. *Organs of neck:* The cervical and tracheal glands are considerably swollen, pulpy, edematous, apparently injected. Thyroid, no abnormalities. Larynx and trachea present a striking picture, the epithelium practically entirely gone. Attached to the underlying submucosa which lines the considerably injected lower portion of the trachea there is a layer of exudate,

friable and elastic, like that in the bronchi and about 1.5 mm. in thickness. This exudate practically forms a cast of the trachea and of the greater portion of the larynx. Both vocal cords are covered. There are, however, several islands uncovered by exudate in the larynx. The exudate is coherent and strips quite readily in one mass from the walls. The process is quite similar at the base of the tongue and at the upper portion of the esophagus down to the level of the mid-portion of the thyroid cartilage. Tonsils, buried, cryptic, and somewhat scarred, in part pulpy. Crypts in general clean. *Alimentary tract*: There is some suggestion of pigmentation of the pharyngeal epithelium in patches in the mid-portion. There is considerable digestion of the gastric mucosa and toward the pylorus, apparently ante-mortem, small hemorrhages below the mucosa. No other abnormalities in the tract. Mesenteric glands are somewhat swollen. The remaining organs show no significant lesions.

Microscopic examination.—*Trachea*: There are patches of a very thick fibrinopurulent membrane still adherent. The injury to the subepithelial connective tissue has been very deep in some places extending almost to the cartilage. In other places, the preserved tissue is thicker, but edematous, and hemorrhagic, with exudate of fibrin and polynuclears. In those areas where the destruction was greatest, the mucous glands have practically disappeared, only a few atrophic acini remaining. The original epithelium has doubtless been destroyed, but a new layer of flattened and highly atypical cells, apparently derived from the mucous ducts, is interposed in places between the edematous subepithelial connective tissue and the overlying membrane. The new cells are pale and hydropic; many of them have pale nuclei of excessive size. *Bronchi*: The changes are like those in the trachea. The lumen of one of the larger branches is almost obstructed by the thick partly detached membrane. The wall of the bronchus is thickened by inflammatory changes, but in the deeper portions between the cartilage rings there is active growth of new connective tissue. There is almost complete reinvestment with atypical flattened epithelial cells like those in the trachea, but they seem to be leading a precarious existence, many of them showing evidence of degeneration. Some of the medium sized bronchi are greatly thickened by an active growth of granulation tissue about them. This fuses into the organizing tissue about the arteries, where they are juxtaposed. There is no obvious dilatation. Organization of the fibrinous exudate in the edematous interlobular septa is also in progress, many fibroblasts and occasional new forming vessels being found. *Parenchyma*: There are confluent areas of lobular pneumonia. The exudate contains many well preserved polynuclears in places mixed with fibrin or coagulated serum. It is not hemorrhagic. There is no organization and no obvious epithelial proliferation. The bronchioles and atria are lined with well preserved, though often desquamated, ciliated cells. They are filled with purulent exudate.

CASE 54.—R. G., 93377, Corpl., Co. D, 166th Inf. Died, October 8, 1918, at Justice Hospital, Toul. Autopsy No. A-8. Autopsy, October 8, — hours after death, by Capt. Jean Oliver, M. C.

Clinical data.—Gas intoxication, mustard-gas, severe, incurred October 1.

Anatomical diagnosis.—Second degree burns of eyes, mouth, and scrotum. Fibrinopurulent tracheitis, bronchitis, and bronchopneumonia. Marked hyperemia and edema of the lungs.

A full autopsy report is not available. The following is a description of the gross specimens received at the experimental gas field.

Gross findings.—*Left lung*: In the upper lobe there are small groups of abscesses beneath the pleura with overlying fibrinous pleurisy. Bronchi to these areas show slightly dilated lumina and in the terminal portions are less severely injured than the larger bronchi. There is no extensive false membrane. Lower lobe shows lobular pneumonia with beginning pleurisy. One bronchus shows thickened opaque mucosa (squamous epithelium?). *Right lung*: Shows scattered areas of fibrinous pleuritis. Necrosis of bronchial epithelium and false membrane do not extend beyond the second branching, outside of which the mucosa is both hyperemic and smooth. Lumina contain fibrin plugs. There is marked patchy edema, and hemorrhage and atelectasis about the smaller bronchi.

Microscopic examination.—*Trachea*: The epithelium is desquamated and necrotic. The denuded surface is covered with necrotic pus cells and fibrin. *Larger bronchi*: The surface epithelium is wholly lost. Bronchus is lined with necrotic material upon which are flakes of adherent slough. Superficial tissue is elsewhere invaded with polynuclears, the nuclei of which become progressively fragmented as they approach the surface. Bacteria are

chiefly Gram-positive cocci, which are plentiful on the surface and in the adherent slough. The submucosa is edematous and infiltrated with wandering cells, among them many polynuclears and many fibroblasts. Vessels are intensely congested, not thrombosed. Mouths of the ducts of the mucous glands contain exfoliated cells. Cells lining the ducts are of the flat squamous type and tend to creep over the adjacent tissue. Adherent lymph node shows caseous foci. Inflammation of submucosa extends between the cartilages to involve the periglandular areolar tissue. There is much inflammatory exudation, fibrin, etc., and a focal area of suppuration in which no bacteria are demonstrable. *Medium-sized bronchus:* Is lined with membrane composed of dense layers of leucocytes enmeshed in a fibrin network. Bacteria, chiefly Gram-positive cocci, in small groups (staphylococcus) are abundant throughout this layer. The bronchial wall itself is edematous and shows inflammatory infiltration. The adjoining alveoli are filled with dense plugs of fibrin, passing over from one alveolus to another. In it are a few desquamated alveolar cells and leucocytes. External to this, the alveoli are collapsed and there is abundant hemorrhage. *Lung:* The epithelium of the terminal bronchioles and infundibula is well preserved. There is a great variety in the contents, as in the alveoli. In some alveoli, the exudate is more or less homogeneous. In others the coagulum is mixed with fibrin, red blood cell, etc. Some alveoli are filled with desquamated pigment-containing cells. Capillaries are congested. There is no periarterial edema. Section through *eyelid:* There is a superficial desquamation of the epidermis at the junction of the epidermis and mucous membrane. There is partial necrosis with edema, hemorrhage, and leucocytic infiltration of the underlying corium. The hair follicles show varying degrees of necrosis.

NOTE.—The duration of life after gassing was eight days. Findings were typical of severe mustard-gas burns of skin and respiratory passages. There were very early attempts at regeneration in the trachea and lungs. The lungs showed suppurative foci and in one area there was slight bronchiectatic dilatation.

CASE 55.—W. B., 1025112, Corporal, Co. G, 34th Inf. Died, November 8, 1918, at Base Hospital No. 87. Autopsy No. 5. Autopsy, November 9, — hours after death, by Maj. M. C. Farr, M. C., and Lieut. H. H. Robinson, M. C.

Clinical data.—Severely gassed with mustard gas on October 31, 1918. Symptoms began with dyspnea and vomiting. Later, moist bubbling râles throughout.

Anatomical diagnosis.—Slight mustard-gas burns of serotum. Extensive pigmentation. Fibrinous and necrotic pharyngitis, laryngitis, and tracheitis. Purulent bronchitis. Peribronchial pneumonia. Acute fibrinous pleurisy. Intense edema and congestion of lungs.

External appearance.—There is deep brownish pigmentation of skin of face, neck, scalp, shoulders, back, and flexor surface of arms. There is an apronlike patch over the abdomen and a triangular area with apex downward at pubis, extending over genitalia and anterior aspects of the thighs. There are some slight erosions and thickening of the skin over serotum.

Gross findings.—*Pleural cavities:* There is no free fluid. There are a few fresh adhesions over the right lower lobe. *Heart normal.* *Lungs:* Are voluminous and heavy, and do not collapse. Firm and elastic on palpation, especially at the bases. On section, of a uniform appearance. Diffuse copious edema. No definite pneumonic areas. Drops of pus can be expressed from the bronchioles. There are patches of fibrin over the posterior surface of both upper lobes and over the entire right lower lobe. *Organs of neck:* Tonsils are scarred and fibrous. Pharynx is reddened and there are a few small necrotic membranous patches. Epiglottis, larynx, trachea, and bronchi are covered with an adherent necrotic membrane, somewhat patchy in its distribution. *Alimentary tract normal.* The remaining organs show no lesions of interest.

Microscopic examination.—*Trachea:* The epithelium is completely destroyed. There is a pseudomembrane consisting of fibrin network in which are numbers of polynuclear leucocytes and in some areas numerous bacteria. Submucous layers are edematous, vessels are congested, and there is infiltration by polymorphonuclear leucocytes and a few lymphoid cells, even as deep as the submucous glands. No metaplasia, regeneration, or fibrosis. *Larger bronchi:* Show the same lesions as the trachea. There is marked peribronchial inflammation with hemorrhage and fibrinous exudate in the alveoli. Terminal bronchioles

show an intact epithelium, which, however, is invaded by leucocytes. There is pus in the lumina. *Lungs*: Show marked dilatation of the terminal bronchioles and infundibula, many of which are completely filled with loose fibrinopurulent exudate. There are strips of apparently well-preserved epithelium lying detached in the exudate or partially investing the walls of the bronchioles. In some bronchi, the necrotic lining is replaced by vascular granulation tissue. The alveolar exudate is of varying composition. There are areas which are emphysematous but entirely free from pneumonic changes. The peribronchial character of the consolidation is very evident. There is no periarterial or perivascular edema.

Bacteriological report.—Cultures from trachea and lungs yield staphylococci and unidentified bacillus.

NOTE.—Typical mustard-gas case of eight days' duration. Extensive diphtheritic necrosis of trachea and bronchi. Characteristic peribronchial lesions, and rather widespread edema. There was an early fibrosis of the bronchial walls and no epithelial regeneration.

CASE 56.—R. L., Pvt., 2088261, Co. A, 355th Inf. Died, August 17, 1918, at Base Hospital No. 42. Autopsy No. 1. Autopsy, August 18, 24 hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Exposed to heavy shelling for 6 hours with yellow, blue, and green cross shells on August 8. Admitted to Field Hospital No. 325, with diagnosis "Gas inhalation, delirious, burns of eyes and genitals." On admission to Base Hospital No. 42, diagnosis of diffuse bronchitis, followed by bronchopneumonia. Respiration labored, inspiration and expiration prolonged. Temperature 103.6°.

Anatomical diagnosis.—Extensive gas burns of skin and superficial mucous membranes, conjunctivæ, lips, and respiratory tract. Membranous and fibrinopurulent pharyngitis, esophagitis, laryngitis, tracheitis, and purulent bronchiolitis. Extensive peribronchial pneumonia. Acute fibrinous pleurisy. Pulmonary edema, marked. Cloudy swelling of liver and kidney. Lymphoid hyperplasia of spleen, intestines, and lymph nodes. Adenomata of thyroid gland.

External appearance.—The skin of the penis and scrotum shows considerable ulceration of the epidermis, associated with desquamation in the neighborhood. The base of the ulcers covered with some seropurulent exudate. The skin about the nose and lips shows considerable ulceration, the base covered by a thick brown scab. There is a similar burn of the mucous membrane of the lips, especially the lower, covered with a thick brown scab. At the bend of both elbows and on the inner aspects of both thighs there are many pinpoint to pinhead sized vesicles filled with clear fluid. No ulceration of these areas. There is, however, some desquamation of the skin. A similar picture presents in both axillæ. *Eyes*: In the skin of both upper lids there are a few superficial ulcerated areas covered by red-brown scabs. The bulbar conjunctivæ are somewhat edematous, considerably injected. There are scattered small deep red hemorrhages. Over the cornea there is a small amount of mucopurulent exudate. Pupils: 4 mm. in diameter. *Ears*: No abnormalities. *Nose*: The superficial ulceration extends into both nostrils, affecting the mucous membrane for a distance of 1 cm. on each side. The ulceration is covered by a brown scab. *Mouth*: Teeth in fair condition. Some slimy, cheesy material over the gums.

Gross findings.—*Pleural cavities*: On opening the thorax, the right pleural cavity contains about 30 c. c. of slightly turbid yellow fluid. There is a small amount of fibrinous exudate over all lobes. In the left pleural cavity about 15 to 20 c. c. of similar fluid. Heart enlarged slightly to the right, right border reaching almost to the costochondral line. On incising the pericardium there are no abnormalities in sac. The parietal pericardium toward the right lung shows a number of tiny deep-red hemorrhages. *Heart*: Weighs 325 grams. Right auricle and ventricle dilated. Left ventricle and auricle contracted. Otherwise, normal. *Right lung*: Middle lobe is imperfectly formed. There is no fissure medially separating it from the upper lobe. All lobes are voluminous. The upper lobe and upper portion of the middle are cushiony and inelastic. The lower portion of the upper lobe and the lower lobe are soggy and solid. The pleura everywhere except medially, and here also, in places, is glazed and covered by small amount of fibrinous exudate. Vessels at the hilum; no abnormalities. The bronchial lymph nodes are greatly swollen, pulpy, edematous, deeply injected, pigmented. *Bronchi*: The mucosa shows considerable ulceration. The underlying sub-

mucosa is intensely injected, somewhat swollen. Covering intact and ulcerated mucosa; there is a large amount of fibrinous and fibrinopurulent exudate, which in places forms a membrane. In the smaller branches the lumen is almost occluded. Upper lobe on section presents mottled moist pink and red surface. Air sacs contain a moderate amount of thin frothy fluid. Medially there is a small egg-sized dull reddish-gray patch of consolidation. The tissue is relatively dry and slightly granular. In the posterior and inferior portions of the lobes the smaller bronchi show considerable amount of fibrinopurulent, and more peripherally purulent, exudate. The walls of the bronchioles are injected throughout, and the lung tissue adjoining for a distance of a few centimeters in places is consolidated, grayish red, dry and granular. On section of the lower lobe a moist pinkish-red and deep-red surface presents. Air sacs contain a moderate amount of thin frothy fluid. *Left lung:* Both lobes are more voluminous than normal. The upper lobe, upper portion, cushiony, inelastic. Lower portion, soggy and solid. Lower lobe, soggy, solid patches flat in places. The pleura, vessels, bronchi, and lymph glands similar in appearance to those on the right. The left upper lobe on section presents a mottled pink and red surface. The air sacs contain a considerable amount of thin, frothy fluid. Medially there is a large uniform consolidated area about the size of a large orange. The consolidation resembles gray hepatization. There are no intervening aerated areas. In the mid-inferior and posterior portions there are areas of peribronchial consolidation and larger bronchopneumonic patches. The lower lobe on section presents a red and mottled reddish-purple surface. The changes are similar to those in the right lower lobe. *Organs of neck:* The glands throughout, especially marked in the lower portion, considerably swollen, pulpy, injected. *Thyroid:* Average size, tissue spongy. The acini contain but a moderate amount of colloid. In the right lobe there is a large filbert-sized, sharply circumscribed area, the tissue at the periphery resembling the neighboring tissue somewhat. The architecture is finer, however. The greater portion of the tumor has an almost uniform gelatinous translucent, faintly green-tinged appearance. Near by there is a grape-seed sized mass similar in appearance. *Larynx:* Shows considerable swelling of the mucosa. In places, especially about the true vocal cords, there is some ulceration of the mucosa. The picture throughout the trachea is similar. Covering intact and ulcerated mucosa, there is an adherent membranous mass of fibrinous and tenacious fibrinopurulent exudate. The process is similar in character and almost as extensive in the upper esophagus, posterior pharynx, and base of tongue. The mucosa and deeper tissues here are considerably swollen, mucosa greatly injected. In places there is some ulceration, and covering it there is fibrinous and fibrinopurulent exudate. *Tonsils:* Somewhat enlarged, buried. On section there is a small amount of lymphoid tissue present. There is some scarring. Some of the crypts contain inspissated material. *Alimentary tract:* Esophagus below the area mentioned above shows no abnormalities. *Stomach* shows considerable post-mortem change. *Duodenum, jejunum, and ileum:* No abnormalities, except that the lymph tissue is somewhat more prominent than normal. Toward the lower end of the ileum the Peyer's patches have a shaven-beard appearance. Mucosa everywhere intact. *Appendix* shows some injection of the mucosa toward the distal end. The cecum is considerably dilated. The lymphoid tissue in the cecum and large intestine is somewhat more prominent than normal. No other abnormalities of the colon or rectum. Mesenteric glands are somewhat enlarged, pulpy. Some show moderate injection. *Liver:* There are focal areas of fat infiltration. The remaining organs show no significant changes.

Microscopic examination.—Trachea: Shows a thick fibrinous membrane still adherent in places. Fibrin threads ramify in the superficial portion of the submucosa. Bacteria, chiefly Gram-positive cocci, on surface. Polynuclear infiltration with mononuclears predominating in deeper tissues. Congestion is marked, but there is little hemorrhage. Epithelium is destroyed even in the ducts of the mucous glands. *Lung:* There is an infarct-like area at the margin of which the lung tissue shows merely intense congestion and slight alveolar hemorrhage. In the infarcted area, the medium sized bronchi show a necrosis of the bronchial wall down to the cartilage. They are found with thick membranes, composed of meshwork of coarse fibrin, including nuclear fragments and bacterial masses. What remains of the lumen is filled with masses of degenerating leucocytes-bacteria, and the necrotic wall of the bronchus is infiltrated with pyknotic leucocytes. One dilated infundibulum is filled with a plug of fibrinous material, of loose mesh, with leucocytes. About the necrotic bronchi there

is intense hemorrhage, in places with necrosis of the alveolar septa and decolorization of blood cells. At the periphery of the infarct are groups of alveoli filled with pneumonic exudate; many bacteria, cocci predominating.

Bacteriological examination.—Cultures of *trachea*: *Staphylococcus aureus*, streptococcus nonhemolyticus. Gram-negative bacilli. *Lung* same flora as *trachea*.

NOTE.—The duration of life after gassing was nine days. The case illustrates a very severe type of mustard-gas injury with necrosis in many of the bronchi, involving the entire wall, and leading to extensive hemorrhage in the adjoining tissue. It is by the confluence of such adjacent hemorrhagic areas with subsequent necrosis of the more central portions, and a reaction of the fixed elements at the periphery, that the infarct-like areas described, are formed. There was a massive bacterial infection in the walls of the necrotic bronchi. The injury was so intense that even the cartilages in some of the bronchi were destroyed. Because of the complete loss of all of the epithelial elements, including the ducts of the mucous glands, no regeneration took place.

CASE 57.—W. J. B., 91290, Pvt., Co. K, 165th Inf. Died, March 29, 1918, at 6.45 a. m., at Base Hospital No. 18. Autopsy No. 51. Autopsy, 10 hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Gassed on March 20. On admission, severe conjunctivitis, second degree burns of right eye, nose, forehead, nasal mucosa. Pulse rapid. General rales. March 24, elevated temperature. No definite consolidation. Pain in chest. Respiration difficult. From this time until death temperature remained above 102°.

Anatomical diagnosis.—Mustard-gas burns of skin, conjunctivæ, nasal and buccal mucosa, scrotum. Membranous esophagitis, laryngitis, tracheitis, and bronchitis. Purulent bronchiolitis. Extensive bronchopneumonia. Acute fibrinous pleurisy. Marked pulmonary edema. Cloudy swelling of liver and kidneys.

External appearance.—There are superficial gas burns of the forehead and face, particularly marked over both upper and lower eyelids on the right side. Also present about the left eye and nostrils and lips. There is also a first degree burn of the scrotum. All burns are covered with thick brownish dry scabs. At the bend of the left elbow there is a small recent incision closed with sutures. Superficial glands palpable. *Eyes:* The conjunctivæ on both sides bulbar and palpebral, injected, especially marked on the right. Eyelids on both sides glued together by viscid and caked exudate, most marked on the right side. There are small hemorrhages below the conjunctiva on the right. Right pupil 4 mm. in diameter, left 2.5 mm. The ulceration and scabbing continues about 1 cm. into each nostril. Along the line of closure of the lips, especially the upper, there are small superficial ulcerated areas covered by dry brown scabs. Internal to this, however, the buccal mucosa is pale and delicate.

Gross findings.—*Pleural cavities:* On opening the thorax a number of fibrous adhesions found over the posterior portion of the right lower lobe. Somewhat more numerous at the apex. Also a number of fibrous adhesions over the posterior portion of the lower left lobe, binding the left to the diaphragm. The heart is enlarged somewhat to the right. *Heart:* Weighs 335 grams. The right auricle and ventricle somewhat dilated. Myocardium is of good color, somewhat boiled in appearance. *Lungs:* Right weighs 715 grams. Left weighs 660 grams. All lobes quite voluminous, cushiony and soggy. In all but the middle lobe solid patches are palpable. The pleura over the posterior and interlobar portions of all lobes glazed and covered by a thin layer of fibrinous exudate. Glands at the hilum enlarged, edematous, injected. The bronchial tree throughout shows extensive necrosis of the epithelium. Islands of intact mucosa are present only here and there. The underlying tissue is considerably injected. There is considerable diffuse extravasation of blood. In some of the larger bronchial branches there is associated with the necrotic epithelium a moderate amount of fibrin. The exudate is membranous. In the finer bronchioles the lumen contains viscid pus. About some of the finer bronchioles, especially in the right lower lobe, there is considerable hemorrhage. Scattered throughout all lobes, most marked in the lower and left upper, there are numerous irregular areas of dull reddish gray and in

places deep-red consolidation. In addition there is much thin frothy fluid in both upper lobes and the left lower. *Organs of neck:* The anterior mediastinal, cervical, and tracheal glands, especially those low down in the neck, greatly enlarged, pulpy, edematous, injected. *Thyroid*, no abnormalities. Acini contain a considerable amount of colloid. In the trachea there is some swelling of the mucosa, with considerable diffuse necrosis of the epithelium. In the lower portion the appearance is moth-eaten. The underlying tissue is intensely injected. Towards the larynx the desquamation and injection is less marked. In the larynx, although the underlying tissue is relatively pale, there is considerable desquamation of the epithelium, and in places associated with this desquamation there is fibrinous exudate. The appearance is that of a true membranous exudate. This is well marked on both true and, to a less extent, on the false vocal cords. A similar appearance is seen in the pockets at the upper end of the esophagus. The pharyngeal tissue about the tonsils is boggy. *Tonsils:* Somewhat buried, show large crypts, most of them filled with viscid or dry purulent necrotic material. *Alimentary tract:* The lymphoid tissue is somewhat more prominent than normal. There is patchy injection of the mucosa of the rectum. The mesenteric glands are somewhat enlarged. There is some injection of the distal one-third of the mucosa of the appendix. *Liver:* Shows focal areas of fat infiltration. Remaining organs show no significant lesions.

Microscopic examination.—*Trachea:* In places ulcerated, in others reinvested with stratified squamous epithelium showing numerous mitotic figures. The epithelium in places is elevated from the basement membrane by a foamy coagulum as if blistered. The subepithelial connective tissue contains lymphocytes in moderate numbers, no polynuclears. It is edematous and all the vessels are very congested. *Large bronchus* shows a very similar picture. There is a metaplasia of the epithelium where present, but a large portion of the connective tissue is bare. There is no membrane or exudate upon the surface. The ducts of the mucous glands are proliferating. A Gram stain shows no fibrin, and only occasional bacteria (Gram-positive rods) on the surface. *Lung:* The bronchioles and atria contain purulent exudate, in which are groups of Gram-positive cocci. They are relined, for the most part with flattened epithelial cells. The alveolar septa appear stout and cellular with the low power. Microscopically, there are numerous round cells and plasma cells in the walls, and occasionally a new growth of fibroblasts. Stout filaments of fibrin are seen, both within the capillaries and between the capillary wall and the epithelium. There are, however, no thrombi. The alveolar epithelium shows widespread changes which are interpreted as regenerative. The cells are elevated, rounded or cuboidal, with deeply staining, sometimes vacuolated, cytoplasm. The epithelium is sometimes elevated by the accumulation of edematous fluid, appearing as granular coagulum. There are multinucleated flattened cells. The alveolar spaces are largely filled with pink-staining homogeneous material, but in spaces this is definitely fibrinous. The fibrin is swollen and stains poorly. In addition there are exfoliated epithelial cells, small and large mononuclears, occasional plasma cells, numerous polynuclear eosinophiles, but rarely a polymorphonuclear neutrophile. Careful search in well-stained Gram section fails to show bacteria in these areas. Here and there are strands of fibroblasts growing into the fibrinous exudate. *Spleen* shows nothing of interest except irregular hemorrhage. *Liver:* The cells are swollen and very homogeneous, the capillaries narrowed.

NOTE.—Case of mustard-gas poisoning, dying nine days after gassing. There were well-advanced reparative changes. Trachea and bronchi were lined with stratified epithelium. Small bronchioles and atria still showed suppurative inflammation. There was a widespread regeneration of the alveolar epithelium and a subsidence of the inflammation in the lung, as shown by the large proportion of plasma and mononuclear cells in the septa. An interesting and unusual finding was the presence in some areas of great numbers of eosinophilic polymorphonuclear leucocytes. There was extensive edema, largely fibrinous, and, so far as could be ascertained from a Gram-stained section, unassociated with the presence of bacteria. Aside from the lesions in the trachea and large bronchi, the picture resembled very closely that seen at a corresponding stage of "influenzal" pneumonia. In this particular instance, however, the possi-

bility that a secondary influenzal infection had supervened upon the gassing can be excluded by the fact that the case occurred in March at a time when "influenzal" pneumonia was not prevalent among the troops.

CASE 58.—W. G. S., 107837, Corpl., 5th M. G. Bat., Battery D. Died, June 30, 1918, at Base Hospital No. 15. Autopsy, three hours after death, by Maj. A. M. Pappenheimer, M. C.

Clinical data.—Gassed on June 21, 1918. Admitted to Base Hospital No. 15 on June 26. Diagnosis: Mustard gas. Dyspnea, cyanosis, conjunctivitis, large blebs on back and arms. Temperature, 101°.

Anatomical diagnosis.—Superficial burns on back, shoulders, neck, and scrotum. Conjunctivitis, diphtheritic tracheobronchitis, lobular pneumonia. Pulmonary edema. Fibrinous pleurisy.

External appearance.—There is marked lividity of the head and dependent portions of the body. Eyes show intense conjunctival edema with several fresh hemorrhages beneath the bulbar conjunctiva. There is a bloody discharge from the nares, and a large amount of thin greenish fluid issues from the mouth. Over the neck, shoulder, and upper portion of the thorax there are very numerous superficial elevated blebs, filled with clear fluid. Over the back these have become confluent and the epidermis macerated and lifted up in large sheets, exposing the wet corium. There is no edema of the penis, but the anterior surface of the scrotal sacs shows loss of hair, pigmentation, and superficial desquamation, and was evidently slightly burned. There are no other cutaneous changes.

Gross findings.—*Pleural cavities: Lungs:* The right and left lungs present almost the same changes and can be described together. They are voluminous and heavy, but not extremely so. There are patches of fresh, very delicate, fibrinous exudate, and a few larger sheets of edematous fibrin over the posterior surface of the lower lobe of the right lung. The interlobular septa appear as a translucent grayish network and are obviously edematous. There are a few small areas of interstitial emphysema in the region of the lingula of the left lower lobe. On section there is a very marked edema of all the lobes. A large amount of thin frothy fluid exudes from the cut surface. Here and there are small partially atelectatic patches of a dark red color scattered through the substance of the lung, but there are no extensive areas of collapse. The bronchi appear on section to be filled with purulent exudate and their mucosa in the case of the larger branches covered with slough. They show no obvious dilatation or contraction. Very striking is the surrounding zone, several millimeters in extent, which is darker in color, very translucent and apparently airless and slightly sunken below the adjacent aerated tissue. There are a very few small pneumonic patches scattered through both lungs. These are dry, grayish, granular, and have not undergone suppurative softening. Some of them are surrounded by irregular darker areas of partial atelectasis. In general, there is strikingly little consolidation, the changes being limited to the bronchi.

Heart normal. Alimentary tract: Normal. Histological material lost.

NOTE.—Mustard-gas case of nine days' duration. Gross lesions are very typical. There were the usual cutaneous lesions, and a very intense diphtheritic necrosis of the upper respiratory passages. Lung lesions aside from the widespread edema were almost wholly limited to the peribronchial regions. There were only a few small patches of focal pneumonia.

CASE 59.—F. C., 1526296, Pvt., Co. H., 147th Inf. Died, October 23, 1919, 11 p. m. at Base Hospital No. 45. Autopsy, 28 hours after death, by Lieut. Perry J. Manheims, M. C.

Clinical data.—Gassed with mustard gas at 6 a. m. on October 14. Subsequent information based on Chemical Warfare Service reports. Co. H, 147th Infantry, was exposed on October 12 to mustard-gas bombardment of 2,000 150-mm. shells. October 18, developed bronchopneumonia. Condition serious. Clinical diagnosis: Bronchopneumonia, following inhalation of mustard gas.

Abstract of anatomical findings.—Small hemorrhages in both conjunctivæ. Characteristic burn of scrotum. Pigmentation of skin of inner side of thighs. *Heart normal.*

Gross findings.—*Pleural cavities:* Left contains no fluid or adhesions. Right shows fresh fibrinous adhesions between the lobes. *Left lung:* Is reddish grey in color. On section, it is hyperemic with areas of consolidation. *Right lung:* There is a small sear with three small partly calcified nodules. The upper lobe in general is grey in color, generally crepitant with a few small areas of consolidation. The middle and lower lobes are the same. *Stomach and small intestines* contain a few hemorrhagic areas. *Large intestine* normal. *Larynx and trachea:* Erosions of the mucosa with general hyperemic color and hemorrhagic areas. The remaining organs show nothing of interest.

Microscopic examination.—No section of trachea preserved. *Large bronchi:* Desquamation or complete necrosis of the epithelium. Exudate of polymorphonuclears, epithelial cells and bacteria in the lumen. Extensive congestion of bronchial vessels. Edema of walls and of peribronchial tissue. There is a loose leucocytic infiltration. *Lungs:* Show intense congestion of all capillaries, hemorrhages into alveoli, numerous pigment containing cells, very little fibrin. Fresh fibrinous exudate on pleura. Another section shows a definite suppurative focus with necrosis and masses of bacteria, destruction of alveolar septa, etc. There is marked periarterial edema. Section stained for bacteria shows numerous Gram-positive cocci, some in long chains, but chiefly confined to bronchial exudate.

Bacteriological examination.—Heart's blood at autopsy showed long chained hemolytic streptococcus. Culture from lung showed hemolytic streptococcus.

NOTE.—Mustard-gas case of nine days' duration. No special features of interest. No reparative changes noted in section. There was an obsolete apical tuberculosis, which did not appear to have been activated by the gassing.

CASE 60.—J. L., 44533, Corpl., Co. M, 16th Inf. Died, October 10, 1918, 9.45 a. m., at Base Hospital No. 15. Autopsy, six hours after death, by Maj. Rolfe Floyd, M. C.

Clinical data.—Mustard-gas inhalation and contact, received in action October 1, 1918.

Anatomical diagnosis.—Extensive mustard-gas burns of skin. Diphtheritic laryngitis, pharyngitis, and bronchitis. Edema and congestion of lungs. Peritoneal and pleural adhesions.

External appearance.—Extensive first degree burns and desquamation of epidermis over upper part of chest and almost whole of back. Burns of first and second degree about lips, nostrils, and eyelids. No burns of scrotum or buttocks.

Gross findings.—*Peritoneal cavity:* There are extensive old organized adhesions, binding together the abdominal viscera. *Pleural cavities:* The left is obliterated by fibrous adhesions. The right also shows fibrous adhesions less dense than on the left side. *Left lung:* There is extensive bronchopneumonia in the lower lobe with areas of intense hemorrhagic exudate. Consolidated areas are numerous but not confluent. Small bronchi contain pus. The unconsolidated lung is very edematous and congested. *Larger bronchi* show extensive diphtheritic necrosis extending down through the medium-sized tubes. In the lower lobe there are small calcified and fibrous nodules surrounded by sear tissue. Lymph nodes at hilus contain small caseous nodules. *Right lung:* Shows extensive edema and congestion with areas of diffuse consolidation. No tuberculous foci. *Organs of neck.*—*Pharynx, uvula, and tonsils:* Show a diphtheritic membrane which extends down the entire length beyond the trachea into the bronchi. False membrane is yellow in color and fairly tenacious, still adherent. Esophagus beyond the pharynx is normal. *Stomach and intestines:* Areas of acute congestion. Abdominal vessels are congested. *Kidneys* show old infarcts. The remaining organs are normal.

Microscopic examination.—*Trachea:* No sections. *Medium-sized bronchi:* Are lined with a thick fibrinopurulent membrane. Entire bronchial wall is infiltrated with leucocytes, the nuclei of which are pyknotic. *Lungs:* The terminal bronchioles contain an exudate which in some is composed almost entirely of polymorphonuclears, in others of a granular coagulum. The lining epithelium is in general well preserved, though the desquamation in places is probably the result of post-mortem change. The exudate about bronchus is largely fibrinous and hemorrhagic. There is no organization in progress. Elsewhere there are patches of lobular pneumonia, not definitely in relation to bronchi, and surrounded by an edematous zone. An interesting histological feature is the lifting up of the pleura, with its intact

mesothelial cells, by a layer of edema. Section stained for bacteria shows few cocci in bronchial exudate, and practically none in the parenchyma. *Liver, spleen, and kidney* show no significant lesions.

NOTE.—Typical mustard-gas case of nine days' duration with extensive diphtheritic necrosis of trachea and bronchi, large areas of bronchopneumonia and pulmonary edema. No special features except perhaps the absence of reparative changes.

CASE 61.—M. M., 3105447, Pvt., Co. C, 109th Inf. Died, October 11, 1918, 8.55 a. m., at Base Hospital No. 42. Autopsy No. 53. Autopsy, six hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Gassed October 2, 1918, bled at Field Hospital No. 110. Contact burns of face, scrotum, penis, and thighs. Conjunctivitis and laryngitis. On admission, respiratory distress, general râles, heart enlarged to right. Accessory muscles of respiration active, chest hyperresonant, expiration prolonged. *Clinical diagnosis:* Gas inhalation and contact burns, emphysema, cardiac dilatation, and bronchopneumonia.

Anatomical diagnosis.—Superficial gas burns of conjunctivæ and skin. Acute pharyngitis, laryngitis and esophagitis, tracheitis and bronchitis. Peribronchial pneumonia of all lobes. Pulmonary edema. Cardiac dilatation of right side. Cloudy swelling of liver and spleen. Detailed protocol not received.

* *Microscopic examination.*—*Trachea:* There is a dense membrane firmly attached to the adjacent tissue. Epithelium in general is wanting, in places there is a single row of flattened cells beneath the slough. Leucocytic infiltration is moderate and accompanied by pyknosis and fragmentation of the nuclei. There is marked hyperemia and hemorrhage. Epithelium of mucous glands is desquamated, and the cells of the ducts show proliferation and mitotic figures. (See fig. 15.) There are numerous bacteria on the surface. *Bronchi:* There is complete epithelial necrosis. Many bronchi are filled with purulent exudate and bacteria. In many places the entire bronchial wall is involved as well as the adjacent alveoli, so that these are practically small abscesses. About these gangrenous zones there is hemorrhage. A few of the bronchi show regenerating new epithelial cells being interlaid between the still adherent membrane and the granulating submucous tissue. *Lungs:* Edema is marked and diffuse in two of the blocks. A third block shows no edema but marked emphysema and dilatation of the infundibula together with bronchopneumonia of the usual type. In some places, especially in the vicinity of the inflamed bronchi, the exudate is fibrinous, in others a uniform coagulum. In places there are definite abscesses with masses of bacteria, which appear to have originated in the distended atria, but involve the adjoining tissue. *Pharynx:* The section passes through localized areas in which the epithelium is replaced by an adherent superficial slough, the base of which shows an acute leucocytic infiltration. (Fig. 31.) A section of *skin*, probably from the scrotum, shows a partial desquamation of the superficial squamous cells with vacuolar degeneration of the upper layers. There are some areas in which there is total necrosis of the entire epithelium, with edema and leucocytic infiltration of the corium. In the ulcerated areas the pigment in the rete mucosum is clumped and there are numerous chromatophores. There is no evidence of regeneration at the margins of the ulcerated areas. *Kidney and liver* show cloudy swelling. *Adrenals* are congested.

NOTE.—Mustard-gas case, dying nine days after exposure. Severe destructive lesions of the upper respiratory tract extending into the smaller bronchioles. There was widespread hemorrhagic edema, lobular pneumonia, and suppurative foci, probably originating in the smallest bronchioles or atria. The evidences of repair were very slight, being limited to the earliest proliferation of the epithelium in the larger bronchi.

CASE 62.—O. H., Corpl., 45273, Hdqrs. Co., 18th Inf. Died, October 11, 1918, at 4 a. m., at Base Hospital No. 18. Autopsy No. 128. Autopsy, October 11, 14 hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Gunshot wounds of right arm and hip, with subsequent gas bacillus infection. Gas inhalation incurred in action October 2.

Anatomical diagnosis.—Extensive gunshot wounds of upper right arm, with infection. Gunshot wounds of right buttock. Healing conjunctivitis and superficial burns of skin. Infected burn of scrotum. Healing gas burns of upper respiratory tract. Small areas of organized pneumonia especially marked in right upper and lower lobes. Few small bronchiectatic cavities, filled with exudate. *Ascaris lumbricoides*. Healed and recent ulcerations of lower ileum and cecum, possibly due to worm. Localized fibrinous peritonitis.

External appearance.—Externally there is a large wound of the right upper arm 15 by 8 cm. The shoulder and anterior chest in the neighborhood are puffy. On palpation a considerable amount of gas is felt. The wound shows necrotic injected muscle in the base. A thin watery grayish-black exudate in small amount in places. On pressure of the wound crepitation is made out. The neck, axillary folds, and abdomen show numerous tiny vesicles filled with clear fluid. In the axillary folds there is some bloody pigmentation of the skin.

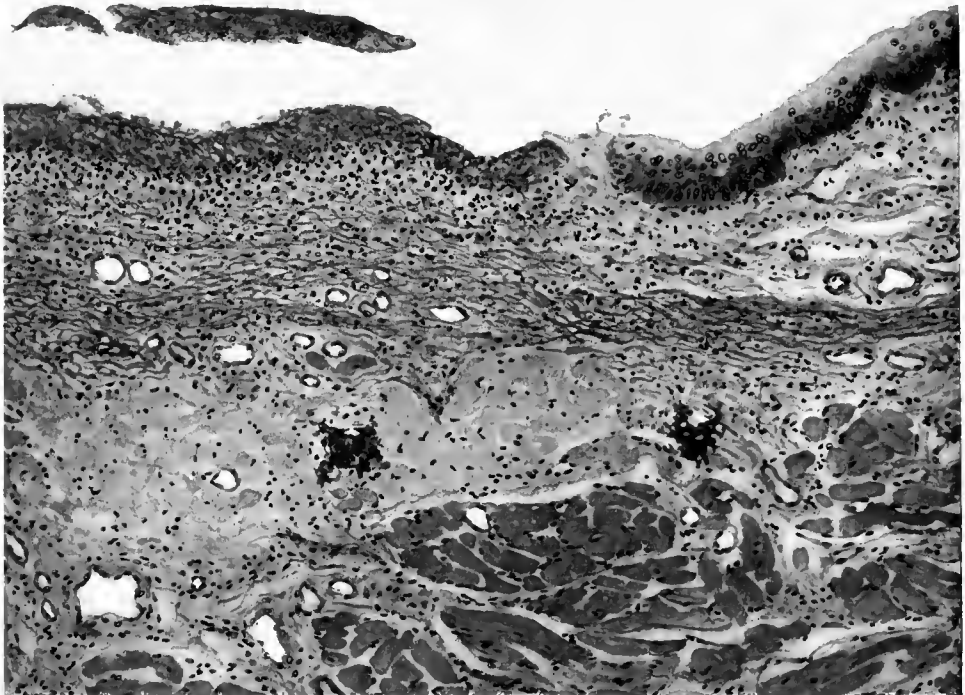


FIG. 31.—Case 61. Mustard-gas burn, 9 days' duration. Pharynx. Localized superficial necrosis of epithelium with inflammatory reaction

The scrotum, penis, toward the head, show superficial ulceration of the epidermis and some matted seropurulent exudate. *Eyes:* The outer corners are glued together with matted exudate. Over the right buttock, upper portion laterally, there is a wound in the skin about 6 by 4 cm. extending into the muscle. In the skin of the left ankle there is a large irregular bleb filled with thin fluid.

Gross findings.—*Peritoneal surfaces:* In the right hypochondrium show patchy injection and small hemorrhages. The hepatic flexure of the colon glued to the liver by fibrinous exudate. There is considerable post-mortem discoloration, greenish black in the neighborhood. The stomach is considerably distended with gas. *Pleural cavities.*—*Right lung:* The lobes are voluminous and cushiony in great part. The pleura is thin. The glands at the hilum are somewhat enlarged, pulpy, and seared. There is slight to moderate diffuse injection of the mucosa. In the lumen there is thin fluid. The upper lobe, on section, in great part is well aerated and pink. Toward the apex there is considerable scarring. There are strands

and small nodules of firm gray tissue. In one place there is a small pea-sized calcified nodule. Toward the apex there is a bronchus showing considerable dilatation, filled with coherent mucopurulent fluid. On tracing the bronchi from the hilum they are found to become stenotic quite quickly. At one place near the pleura there is a pea-sized yellow, opaque, cheesy mass involving the bronchial lumen and wall. On repeated section, dilated and stenotic bronchi, with small pigmented firm gray streaks and nodules are found, in the posterior portion of this lobe, suggesting the end result of gas inhalation. The middle lobe on section fairly well aerated, pink-red. Throughout the lobe there are firm gray strands and flat nodular areas, a few millimeters in diameter. The picture suggested tiny organized areas following rather extensive peribronchial consolidation. The walls of the bronchi themselves are not appreciably thickened. In general the lumen is considerably smaller than the average. In this lobe, the air sacs contain a moderate amount of thin frothy fluid. *Left lung:* Both lobes fairly voluminous and cushiony. The artery at the hilum shows no abnormalities of its larger branches. The bronchi and glands are similar to those on the right. On section of the upper lobe toward the apex and elsewhere, firm gray streaks and small nodules suggesting organized pneumonia are seen and peribronchial thickening. The lower lobe on section, in general similar to the upper. *Liver* weighs 2,000 grams and shows marked fatty infiltration. *Spleen, kidneys, adrenals, and bladder* normal. *Organs of neck.*—*Thyroid:* Average size and presents no abnormalities. There is considerable colloid present. *Larynx and trachea:* There is much viscid exudate in the lumen. Toward the bifurcation there is patchy injection of the mucosa. The base of the tongue, posterior pharynx and upper esophagus as far as the level of the cricoid cartilage show a uniform thickening of the mucosa. *Tonsils:* Show a moderate amount of pulpy pale lymphoid tissue, somewhat scarred. *Alimentary tract:* The esophagus shows some dilatation. The stomach is considerably distended with gas and contains about 200 to 300 c. c. of bile-tinged contents, partially digested. In the lower ileum there are several apparently healed ulcerated areas in the neighborhood of the valve. The cecum and ascending colon show a number of ragged perforations of the mucosa. In one place the ulceration is about 1 cm. in diameter, the edge heaped upon the base formed by the muscle. Just beyond the ileocecal valve there is a ragged perforation of the mucosa. The serosa and outer muscular coats dissected up for a considerable distance forming a cavity about 3 cm. in diameter, communicating with the interior of the gut by the perforation mentioned above. The walls are moth-eaten in appearance, apparently the habitat of the ascaris mentioned above. It is over this region that the fibrinous exudate mentioned above is found. The remainder of the tract shows no abnormalities.

Microscopic examination.—*Large bronchus:* Covered for the most part with one or two layers of flattened cells, very pale and large with distinct cell membrane. Individual cells show pyknosis of nuclei and hyaline condensation of cytoplasm. The superficial portion of the subepithelial tissue is very dense, the membrana propria and collagen fibres are swollen and indistinct. There are very few wandering cells in this zone; the connective tissue and endothelial nuclei are large and succulent. Deeper down there is a rather dense infiltration of lymphoid and plasma cells, especially about the mucous glands. The ducts show the usual epithelial proliferation, with occasional mitotic figures. *Lungs:* Two blocks examined. In one there are definite encapsulated areas with smaller tubercles at the periphery. The granulation tissue at the margin of the tuberculous area is intensely injected, and in one place there is an extensive fresh hemorrhage. The caseation involves the wall of an adjacent pulmonary artery. The section passes through a small bronchiectasis which is situated in the scarred tuberculous area. Elsewhere there is a suppurative bronchiolitis and infundibulitis, with involvement of the adjacent alveoli. The smallest bronchioles are filled with pus and have lost their epithelium. Their wall shows a good deal of fibrous thickening, and the lumina appear narrowed. The remaining part of the lung tissue shows nothing of special interest. The capillaries are congested; there is moderate diapedesis and edema, and here and there alveoli containing leucocytes and fibrin. There are various types of bacteria in the bronchial exudate. Gram-positive cocci predominating.

NOTE.—Mustard-gas poisoning of nine days' duration, complicated with multiple gunshot wounds. The cutaneous lesions are typical, and the trachea and bronchi showed unmistakable evidence of previous gassing with very early reparative changes. There were associated obsolescent tuberculous

lesions in the lung, to which were probably due the small bronchiectases and scars described in the protocol. It is not probable that the gas bronchitis after nine days could lead to the formation of bronchiectasis, and in support of this idea is given the histological study, which shows at least one dilated bronchiole in definite relation to the tuberculous focus. Of interest, in view of the possible activation of old tuberculous foci by exposure to gas, is the intense congestion and hemorrhage about the tuberculous areas. It is conceivable that such a hemorrhage might favor the extension of the tuberculous foci.

CASE 63.—J. W. H., 1627698, Corpl., Co. M., 109th Inf. Died, August 19, 1918, at Base Hospital No. 46. Autopsy No. 7. Autopsy, two hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Date of gassing not known. Admitted to hospital August 10. Cyanosis, air hunger, cough, abundant mucopurulent sputum. Somewhat relieved by venesection. On fifth day, temperature 104°. Dullness, and bronchial breathing. From then until death, periods of improvement; temperature up to 106°.

Anatomical diagnosis.—Extensive gas burns of skin, in part infected, in part healed, associated with local pigmentation. Acute ulcerative laryngitis, tracheitis, bronchitis. Purulent bronchiolitis. Extensive bronchopneumonia. Fibrinous pleurisy. Pulmonary edema. Miliary tuberculosis (obsolete) of bronchial lymph nodes, lung, liver, and spleen. Rupture of right rectus muscle with hemorrhage.

External appearance.—The skin in general has a sallow appearance. In addition, the face, neck, and upper portion of the body has a somewhat bluish cast. The skin of both arms almost to the wrists show extensive areas of superficial ulceration and desquamation. In places there is a small amount of matted skin and purulent exudate over the ulcerated areas. The ulceration extends only into the dermis. There is similar ulceration and desquamation of the skin in both axillae and upper backs. The head of the penis and body show similar ulceration, with some purulent exudate. Over both buttocks, in the right axilla, the outer aspect of the right thigh, there are a number of old ulcerated areas varying in size from a few millimeters to several centimeters in diameter, practically healed, showing new epidermis with brownish pigmentation about them. There are large blotches of brown pigmentation of the skin over the chest and thighs. Associated with all these there are innumerable tiny vesicles filled with clear fluid. The skin of the neck and a portion of the face and scalp shows considerable desquamation. The superficial lymph glands are somewhat enlarged. *Eyes:* Eyelids are somewhat edematous toward the inner canthus. On each side there is a small superficial ulcerated area covered by a reddish-brown scab. There is some desquamation of the skin of the lids. Conjunctivæ are pale. The pupils a few millimeters in diameter. *Nose:* In both nostrils there are superficial ulcerated areas, covered by scabs. In the nose there is a moderate amount of mucopurulent secretion. *External genitalia:* No addition to the note above. The skin of the scrotum in two places shows healed superficial areas. Attached to the new epidermis there is some desquamated epithelium.

Gross findings.—*Abdomen:* On opening the abdomen, the peritoneal surfaces in general are delicate and pale. In the region of the attachment of the internal rectus on the left, the peritoneal surface shows extensive deep red hemorrhage. In the pelvis there is about 30 c. c. of clear yellow fluid. Binding the lateral portion of the right lobe of the liver to the abdominal wall there is a small amount of apparently organizing gelatinous fibrinous exudate. On incising the rectus muscle on the left, a small egg-sized mass of fluid and clotted blood is found. There appears to be a loss of continuity in the rectus muscle about 6 cm. from the attachment to the pubic bone. There is some apparent scarring of the musculature at the point of rupture. The diaphragm reaches to the fifth rib right, fifth space left. *Thorax:* On opening the thorax about 50 c. c. of turbid yellow fluid found in the right pleural sac. There is some fibrinous exudate posteriorly between the lobes and the chest wall. A similar picture presents on the left. There is perhaps but 30 c. c. of fluid here. *Heart:* Enlarged somewhat to the right. Shows no significant lesions. *Right lung:* All lobes of the right lung are very much more voluminous than normal. The upper is cushiony, soggy, many large

solid patches felt. Middle and lower lobes similar, with apparently more consolidation in the upper portion. Pleura everywhere glazed, covered by tightly adherent fibrinous exudate. On stripping this posteriorly, tiny vessels are seen in the pleura below in places only. The vessels at the hilum show no abnormalities. Glands are greatly enlarged, pulpy, edematous, injected and pigmented. Bronchus shows considerable swelling and intense injection of the mucosa. In places there is desquamation of the mucosa. Everywhere there is considerable mucopurulent and fibrinopurulent fluid, blood tinged. On section, the upper lobe, a moist mottled pink, whitish-yellow and yellowish grayish-red surface presents. Air sacs in general contain a considerable amount of thin frothy fluid. Scattered throughout the lobe there is much dull grayish-red consolidation. Patches vary in size from a few millimeters to one large patch having a surface area 6 cm. Associated with these solid patches the bronchioles in places contain viscid purulent matter. The walls of these smaller bronchioles merge with the surrounding consolidation. Middle lobe on section, presents a picture in general similar to the upper lobe. There are numerous areas of consolidation associated with bronchial branches which contain viscid purulent material. There is moderate amount of fluid in the air sacs elsewhere, in this lobe. In places there are dilations of the bronchi towards the periphery. Lower lobe, on section presents a picture in general similar to the other lobes. Here the peribronchial consolidation is much more distinct. There is considerably more injection present. Lower portion of the lobe, on repeated section, the bronchial branches in greater numbers show viscid purulent fluid. The peribronchial consolidation is much more extensive here. The bronchi throughout have a larger diameter than normal. *Left lung:* Both lobes are very much more voluminous than normal, especially the upper, and are quite solid. The lower in the median portion is cushiony. The pleura, vessels, lymph glands, and bronchi similar in appearance to those of the right. On this side the necrotic desquamating mucosa is more conspicuous than on the right side. The upper lobe on section, in general similar to the right upper lobe. Consolidation, however, is much more marked; in places the patches are almost confluent. Associated with the gelatinous areas of consolidation there are also numerous small yellow opaque areas. On section of this lobe towards the hilum, there is an enlarged bronchial lymph gland, showing a pea-sized chalky and calcified mass, encapsulated by firm gray tissue. Left upper lobe, bronchi, and areas of peribronchial consolidation have a greenish color. This is especially true in the centre and the upper portion of the lobe. In places, especially in these areas, the bronchial branches show moderate dilatation. In this lobe, on further inspection there are seen yellowish opaque nodules much firmer in consistence than the consolidation mentioned above. These are especially prominent medially. The left lower lobe on section, in general presents a picture similar to that in the other parts, except that the process medially is less marked. Scattered throughout this relatively well aereated portion considerable numbers of discrete pinhead sized and smaller firm gray nodules. *Organs of neck:* Glands throughout the neck, especially below, greatly enlarged, pulpy, edematous, and injected. Those in the mediastinum show areas of gray scarring, moderately pigmented. *Thyroid:* Marked amount of colloid in the acini. *Larynx:* Shows several areas of ulceration of the mucosa, both of the epiglottis and true vocal cords. The largest patch is 1 cm. in diameter. These ulcerations extend into the cartilage. Elsewhere the mucosa is injected, swollen and covered by loose mucopurulent exudate. *Trachea:* Mucosa is somewhat swollen, and injected, especially towards the bifurcation, where in addition there is considerable desquamation of the epithelium of the mucosa, and associated with these areas there is a moderate amount of adherent fibrinous and fibrinopurulent exudate. In the lumen there is a considerable amount of mucopurulent secretion. *Tonsils:* Are almost gone on the left. On section, however, one crypt filled with viscid purulent material. On the right, the tonsil is buried and crypts are clean. *Alimentary tract:* Mucosa of the pharynx and upper esophagus is slightly swollen, moderately injected. *Stomach:* No abnormalities. *Cecum:* Some patchy injection of the mucosa. Mesenteric glands are slightly enlarged, and pulpy. *Liver:* There are a few minute, encapsulated, caseous areas and focal fat infiltration. No other significant lesions. *Spleen:* Also contains small yellowish nodules, otherwise the appearance of an acute splenic tumor. *Adrenals:* Slight cortical edema, moderate lipid depletion.

Microscopic examination—Skin: There are two blocks, showing hyperkeratosis and thinning of the remaining layers of epidermis. There is marked hyperpigmentation with chromatophores in the superficial layers of the corium. The smaller vessels are collapsed

and empty, surrounded by a loose aggregation of pyenotic lymphocytes and occasional polymorphonuclear cells with distorted nuclei. The section evidently represents a healed pigmented lesion. *Trachea*: There are patches of regenerated stratified non-ciliated epithelium alternating with ulcerated areas to which necrotic membrane is adherent. The ducts frequently contain solid plugs of epithelial cells. Submucosa is edematous and in the ulcerated regions is infiltrated with both polymorphonuclear and mononuclear cells. Where the epithelial regeneration has occurred, the underlying tissue has rather the character of clean granulation tissue. *Lungs*: The bronchi all contain exudate which is chiefly purulent but in some instances is undergoing early organization. Lining epithelium of some of the bronchi is intact, in others necrotic, and still others regenerative and metaplastic. There are the usual peribronchial lesions; areas of extensive peribronchial pneumonia with fibrinous exudate often showing early organization. Alveolar wall in many places is thickened by the presence of numerous large pale epithelial cells having in general the character of fibroblasts, but possibly derived in part from the endothelial cells of the capillaries. One block of lung tissue shows in addition to the thickening, diffuse edema, hemorrhage, and focal areas of suppuration. *Rectus muscle*: There is hyaline necrosis of the fibres with hemorrhage and acute inflammatory reaction. *Liver, spleen, kidney* show no striking changes.

Bacteriological examination: Culture of *lung*: Staphylococcus aureus, large number. Culture of *vocal cords*: Streptococcus, nonhemolytic, non-green-producing.

NOTE.—The case is a typical one of mustard-gas poisoning. The exact duration is not established, but was over nine days. The destruction of the mucosa of the upper respiratory passages was less severe than in many cases, and does not involve the smallest branches, in which, generally speaking, the epithelium appeared to be preserved. Early regeneration occurred. Broncho-pneumonia was extensive but does not appear to be of the typical influenzal type, associated with extreme and widespread hemorrhagic edema.

CASE 64.—F. M., 2209877, Pvt., Hdqrs. Co., 355th Inf. Died, August 18, 1918, 9.45 p. m., at Base Hospital No. 46. Autopsy No. 8. Autopsy, 19 hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Patient was gassed on August 7 to 8, having been exposed to yellow, green, and blue cross shell. On August 15, patient was weak and a little delirious. There was a cough without sputum. Throat was red and edematous. Painful burns of scrotum and face. Râles at the bases posteriorly. August 18, patient became weaker, apprehensive, and at times delirious.

Anatomical diagnosis.—Extensive gas burns of skin and mucous membranes. Acute laryngitis, tracheitis, and bronchitis. Purulent bronchiolitis. Acute peribronchitis. Extensive bronchopneumonia. Acute fibrinous pleurisy. Marked pulmonary edema. Dilatation of right auricle. Obsolete tuberculosis of bronchial lymph nodes. Terminal gas bacillus infection.

External appearance: There is a marked gas burn about the lips, over the left eye, scrotum and penis. Burns of the face extend into the subcutaneous tissues and are covered by a dry red brown scab. The scrotum and penis show in addition to the ulcerated epidermis, moderate amount of matted serum and purulent exudate. There is a small area of ulceration covered by a scab toward the inner canthus of the right eye. There are areas of desquamation of the epidermis over the scalp, about the ears, and in the genital fold. Axillæ, clear. Superficial lymph glands, somewhat enlarged. Conjunctivæ slightly edematous, show patchy injection. There is some mucopurulent secretion present. The corneæ slightly cloudy. Pupils, dilated 6 mm. in diameter. *Ears*: No abnormalities except as above mentioned. *Nose*: In the left nostril there is an area of superficial ulceration covered by a red brown scab. Mucosa is somewhat injected. There is some bloody mucopurulent secretion present. *Mouth*: Lips show ulceration mentioned above. Teeth poorly formed. In the upper jaw, there are several milk teeth present. There is considerable erosion of the cutting edges. A few teeth gone from the lower jaw.

Gross finding.—*Pleural cavities*: On opening the thorax about 60 c. c. of thin blood-tinged turbid fluid found in the right sac. In the left there are a number of delicate fibrous adhesions between the lungs and the chest wall. In this cavity also there are about 40 c. c.

of blood-tinged fluid. Heart is normally disposed. Pericardium is normal. *Heart* is normal except for dilatation of right auricle. *Right lung*: Upper and lower lobes are very much more voluminous than normal, cushiony, soggy. Middle lobe is fairly voluminous, slightly soggy. *Pleura*, especially posteriorly, glazed, covered by small amount of fibrinous exudate. There is considerable reddish-purple discoloration of the pleura, and in addition there are scattered small hemorrhages posteriorly. *Vessels*: No abnormalities, except the pulmonary artery somewhat dilated. *Glands* are moderately enlarged, pulpy, edematous, injected, pigmented, searred. *Bronchi*: There is considerable swelling, injection and hemorrhage of the mucosa. There is much greenish-black discoloration. In the lumen there is a large amount of thin frothy fluid. On section of upper lobe a strikingly moist deep red surface presents. Air sacs are moderately distended with thin fluid. The smaller bronchial branches contain fibrinous and fibrinopurulent exudate; their walls are injected, the surrounding lung tissue consolidated. Posteriorly there is some gelatinous reddish lung tissue, and in addition there are fair-sized areas of granular deep red consolidation. Middle lobe on section shows little involvement, and there are but a few areas of consolidation in this lobe. Lower lobe on section quite similar to the upper, however, the bronchial branches are filled with purulent exudate. Walls are deeply injected. There is much consolidation. In the air sacs there is a striking amount of thin frothy fluid. In addition there is considerable extravasation of blood throughout the tissue and near the apex of this lobe there is an egg-sized solid slightly granular deep red consolidated patch. *Left lung*: Both lobes are more voluminous than normal, especially the lower. The upper, cushiony, soggy. The lower, soggy. *Pleura*: Vessels, bronchi, lymph glands, similar to those on the right in appearance. In addition, lymph glands show numerous yellow opaque nodules. Upper lobe on section is similar in general to the right upper. The lower, in general similar to the right lower. *Liver*: Fatty infiltration and small cystic spaces apparently due to gas-bacillus infection. *Adrenals*: Cortical edema with injection of inner cortical zone. *Organs of neck*: Glands in the lower portion of the neck are moderately enlarged, edematous, pulpy, injected, pigmented, show some scarring. *Thyroid*: Average size. The right lobe is bifurcated. Tissue is pale and spongy. The acini contain a moderate amount of colloid. *Larynx*: There is considerable swelling of the mucosa with patchy injection. There are small areas of ulceration in the epiglottis. There is also some ulceration of the true vocal cords. From the true vocal cords downward the ulcerated and intact mucosa is covered by a considerable amount of slimy, dirty brown exudate. Within and below the mucosa there are numerous deep red hemorrhages, especially toward the bifurcation of the trachea. The greater portion of the brownish exudate is present in the lower portion of the pharynx and the upper portion of the trachea. The adjoining mucous membrane of the base of the tongue and larynx moderately injected. *Tonsils*: Show a small amount of lymphoid tissue. There is considerable scarring of each.

Alimentary tract: Esophagus shows some injection of the mucosa as far as its mid-portion. *Stomach*: No abnormalities. *Jejunum*: Upper portion shows some patchy edema of the mucosa. *Ileum*: Shows areas of patchy injection of the mucosa with which there is associated some extravasation of the blood. The lymphatic tissue throughout is somewhat more prominent than normal. *Appendix, cecum, colon, and rectum*, no abnormalities. Tissue about the rectum and in the bladder wall posteriorly shows numerous dilated, engorged, and in places, thrombosed veins. The mesenteric glands are slightly enlarged, pulpy, and injected.

Microscopic examination.—*Trachea*: There is no pseudomembrane present. Normal epithelium is replaced by layers of polygonal squamous cells resting upon basement membrane. Mucous glands have disappeared. *Large bronchi*: Many show gangrenous lining and hyaline necrosis, not extending very deeply into the bronchial wall. There is abundant hemorrhage both of mucosa and adjacent lung tissue. Some bronchi show regeneration of squamous stratified epithelium. *Lung*: Tissue at a distance from the bronchi shows emphysema and moderate hemorrhagic edema. In the second block numerous sections were taken at different levels and mounted in series. In this way there are demonstrated suppurating cavities directly in connection with bronchi. These suppurative foci are surrounded by areas of organizing pneumonia. In some of the alveoli there is exfoliated ciliated epithelium, probably aspirated from the bronchi. The third block shows complete atelectasis. *Kidney, spleen, liver, and bronchial lymph nodes* show no features of special interest.

Bacteriological examination.—Cultures of *trachea* show streptococcus and colon group organisms. Smear shows Gram-positive and negative cocci and Gram-negative bacilli in *trachea*. Gelatinous and consolidated lung, numerous streptococci, single cocci, and Gram-positive bacilli.

NOTE.—Mustard-gas case, dying nine days after exposure, and presenting typical lesions at autopsy. In the *trachea* there was beginning regeneration. Many of the medium-sized bronchi showed a very severe injury, and the terminal bronchioles were transformed into abscesses with a reactionary zone of organizing pneumonia about them.

CASE 65.—S. R., 2299831, Pvt., Co. H., 112th Inf. Died, November 9, 1918, 3.30 p. m., at Base Hospital No. 87. Autopsy, November 10, 24 hours after death, by Lieut. H. H. Robinson, M. C.

Clinical data.—Gassed on October 31, 1918; 1,000 yellow cross and 400 blue cross and green cross shells used in bombardment, northeast of Xammes. On admission to base hospital, eyelids were red and swollen, photophobia, coughing, slight dyspnea, rapid pulse. Venesection performed on November 3 and 5. Before death pulse became rapid. Whistling râles were heard through the entire left chest.

Anatomical diagnosis.—Pigmentation and superficial burns of skin, neck, scalp about eyelids and lips. Small erosion in fold of skin on right side of scrotum.

Gross findings.—Pleural cavities: There is no free fluid. Easily separated pleural adhesions over both lungs. *Organs of neck: Trachea:* In its upper portion is covered with thick necrotic membrane, which is absent in places exposing the deeply eroded surface. The lining of the lower portion of the *trachea* and the larger bronchi is smooth but bluish in color, as if mucosa had been exfoliated. *Lungs* are voluminous and heavy. On pressure a large amount of frothy blood exudes from the cut bronchi. On section the anterior portions of the lung are air containing. Elsewhere all lobes are full of small firm closely set, but irregularly outlined, patches of consolidation. Cut surface is very moist, and mottled pink and dark red. Blood flows freely from the congested vessels. Smaller bronchi contain thick yellow pus. *Heart* is normal. *Kidneys* show moderate chronic nephritis. Remaining organs show nothing of interest. *Gastrointestinal tract* is normal throughout.

Microscopic examination.—*Trachea:* No pseudomembrane remains. Epithelium is completely destroyed. The submucosa is edematous, congested, and infiltrated with polymorphonuclears and other types of wandering cells. *Lungs:* Two of the blocks show gangrenous necrosis of the walls of the bronchi. Other lumina are completely filled with plugs of fibrino-purulent exudate and bacteria. There is intense edema of the surrounding lung tissue, leading to rupture of the alveolar walls. Interlobular and subpleural lymphatics are greatly distended. Another block shows diffuse lobular pneumonia, with many swollen alveolar cells amongst the exudate. Several other sections show no additional features.

NOTE.—A case presumably of mustard-gas poisoning of nine days' duration. Skin lesions were of moderate severity, but there was very intense necrosis of the respiratory passages, with peribronchial consolidation and widespread edema. Probably because of the complete epithelial destruction, there were no reparative changes.

CASE 66.—P. J. C., 482258, Pvt., Co. L, 54th Inf. Died, November 14, 1918, at 9.45 a. m., at Base Hospital No. 87. Autopsy, November 15, 23 hours after death, by Lieut. H. H. Robinson, M. C.

Clinical data.—Gassed on November 5, 1918, by mustard-gas shell. On admission, difficulty in breathing and many râles in chest. Burns about eyes, face, scrotum, and knees. Epistaxis.

Anatomical diagnosis.—Mustard-gas burns of lips, eyelids, face, penis, scrotum, and knees. Brownish-purple pigmentation on the anterior surface of thighs. Diphtheritic tracheitis and bronchitis. Peribronchial hemorrhages. Remaining viscera, normal. Gastrointestinal tract not recorded.

Microscopic examination.—*Trachea* is covered with several layers of nonciliated epithelium showing occasional mitoses. Some of the ducts of the mucous glands contain actively

regenerating cells and are filled with more or less solid plugs. The submucosa is moderately edematous. There is a loose infiltration of mononuclears and many of the connective tissue cells have the character of fibroblasts. The blood vessels are hyperemic and their endothelium is swollen. *Lungs*: There are extensive fresh hemorrhages in the alveoli and septa, with edema in the surrounding tissue. Some of the small bronchi show purulent exudate and exfoliation of the epithelium. A second, very interesting, but poorly stained section shows a fibroblastic thickening of the septa, with early organization of the alveolar exudate.

NOTE.—Mustard-gas poisoning, with death on the ninth day after gassing. There was well defined regeneration of the tracheal epithelium with beginning fibrosis of the subepithelial connective tissue. There was extensive hemorrhagic edema of the lungs with interstitial fibrosis. This may have been associated with a secondary influenzal infection.

CASE 67.—A. W., 127455, 1 A. M., R. A. F. 3 Kite Balloon Section. Died, October 30, 1918, at 12.50 p. m., at Base Hospital No. 2. Autopsy, two hours after death, by Capt. B. F. Weems, M. C.

Clinical data.—October 21, admitted to No. 5 Casualty Clearing Station. Gas-shell wound of head. October 22, admitted to Base Hospital No. 2. Sore eyes, throat, chest; no vomiting; coughing. Slightly cyanosed; eyelids swollen, eyes congested. Heart normal. *Lungs*: Tracheal and bronchial râles, few fine râles at left base. No burns. October 24, coarse râles have disappeared; fine moist râles at both bases. October 25, foul breath; fine râles generally over anterior chest; expiration prolonged; still slightly cyanotic. October 26, same signs as yesterday. Profuse purulent sputum. No improvement in general condition. Sputum—direct smear—Gram-positive lanceolate diplococci, spirilla, staphylococci. Culture—pneumococcus, Type IV. October 27, feels better. Slight cyanosis. October 29, holding his own, breathing quietly. Generalized fine and coarse râles. Unable to localize consolidation. October 30, marked cyanosis, respiration rapid and feeble, chest filled with moisture. Died at 12.50 p. m.

Anatomical diagnosis.—Membranous pharyngitis, tracheitis, and bronchitis, bronchopneumonia; old pleural adhesions; congestion of abdominal viscera; status lymphaticus; inhalation of irritant gas, presumably mustard.

External appearance.—Stigmata of status lymphaticus. Skin is dusky yellowish-brown, quite soft and smooth. Very little hair over thighs and trunk, feminine distribution of pubic hair. Sparse beard, adenoid facies; teeth carious, many missing; high arched palate. Desquamation of epidermis, dusky pigmentation and congestion about the eyes; dried exudate in the corners; deeply injected conjunctivæ, evidences of recent inflammation. Nasal mucosa injected, external orifices otherwise negative.

Gross findings.—*Pleural cavities*: Obliterated by fibrous adhesions. *Left lung*: Covered by fibrous tags; moderately distended; apex and anterior portion of upper lobe are normal in consistence, posterior portion somewhat firmer, slightly lumpy, lower lobe evidently partly consolidated. Lymph nodes at the hilum are congested. Bronchi display a marked injection, mucous membrane is covered by grayish-yellow, necrotic-looking exudate, which extends down into the smallest radicles; there is a slight amount of bronchiectasis. Upon cut surface, the lung is grayish red, rather irregular, numerous points of grayish color representing the plugged bronchioles. Around most of these is a zone of deep injection or hemorrhage, varying in width. There are several large, almost wedge-shaped areas of deep purple with yellowish patches about the bronchi; small abscesses are present in some of these. There is considerable edema in all of this diseased tissue. There are many yellowish-gray plugs in the small bronchi. *Right lung*: Lymph nodes at hilum are markedly enlarged, deeply congested, slightly spotted, but showing no frank suppuration. The lung is covered by fibrous adhesions and very much lacerated in removal. Bronchi contain the same inflammatory products as on the left side. The lung is less voluminous and shows less evidence of consolidation. The cut surface, however, presents almost the same picture as on the left side; the lower lobe is pale in color, except for the peribronchial changes. There is practically no anthracosis present in the lower lobe, although there is considerable amount in all other parts of the lung. There are many areas of hemorrhagic softening. *Organs of neck*: Tonsils are very small, slightly scarred. *Pharynx*: Reveals a coarse membranous inflammation, the membrane being thick and yellow and rather hard to peel. Very slight injection

is noted, the healing process having evidently begun. *Larynx*: Contains the same sort of membranous exudate, but there is the appearance of regeneration in the mucous membrane. *Trachea*: Is not greatly altered in its upper half, but becomes more congested toward the bifurcation; patches of yellowish-gray membrane are present in the lowest third. *Esophagus* is normal. *Heart*: Left chambers contracted, right flaccid. No abnormalities. *Liver, spleen, kidneys, adrenals, and pancreas* congested. *Stomach*: Post-mortem digestion. *Intestine* not recorded.

Microscopic examination.—*Trachea* and *primary bronchus*, no sections. *Lung*: A medium-sized bronchus is cut longitudinally. It is completely filled with a fibrinopurulent plug,

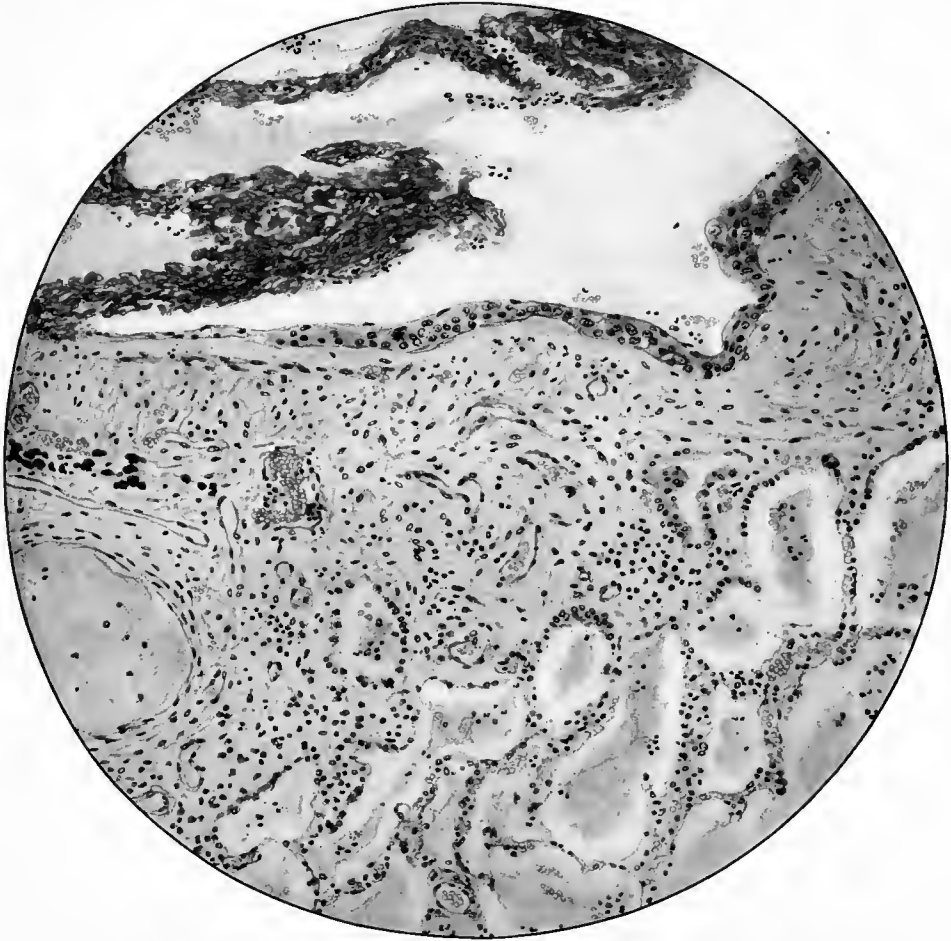


FIG. 32.—Case 67. Mustard-gas burn, 9 days' duration. Section through bronchus, showing regeneration of metaplastic epithelium, fibroblastic thickening of bronchial wall, epithelial proliferation, edema of adjacent alveoli

which in a few places is becoming organized at the point of attachment by the ingrowth of fibroblasts. The outer portion of the plug shows here and there coarse interwoven lamellæ of fibrin. The bronchial wall is represented by a loose vascular granulation tissue, which is covered in places by epithelium, either a single row of flattened cells or several layers of laminated, nonciliated squamous cells. (Fig. 32.) An interesting feature is the presence of sharply outlined areolar spaces within the epithelial cells, containing groups of three or four wandering cells, chiefly small mononuclears. These spaces appear to be formed within the protoplasm of the epithelial cells. Mitotic figures are quite numerous. In the vicinity of the bronchi the alveoli are filled with a hemorrhagic exudate which becomes serofibrinous and finally serous at a distance from the bronchus. The alveolar epithelium, especially in

the neighborhood of the bronchus, appears to be regenerated, and is frequently columnar. In some areas there is epithelialization of the alveolar plugs in progress, as well as fibroblastic growth. Groups of pigment-containing exfoliated cells are present. In addition to these lesions the section shows several circumscribed abscesses, surrounded by a zone of hemorrhage. The purulent center contains large masses of bacteria. The bacterial stain shows great numbers of Gram-negative bacilli and a few Gram-negative coccoid forms in the bronchial exudate, where the staining of the fibrin shows that the decolorization has not been carried too far. Elsewhere bacteria are difficult to demonstrate. Additional blocks show no features beyond those noted. The epithelial proliferation in some of the bronchioles is remarkable, and there are many large atypical cells. *Liver*: The cells in the center of the lobules are atrophic; there is edema between the liver cells and the capillary walls. No other striking change. *Spleen* and *myocardium* normal. *Adrenals* intensely congested; cortex contains very little lipid. There is fair chromaffin staining of the medullary tissue.

Bacteriological examination.—Blood culture: Sterile. Lung culture (blood plate): *Staphylococcus aureus*, pure. Spleen culture: *Staphylococcus aureus* and *pneumococcus*, type?

NOTE.—Death occurred nine days after definite history of inhalation of irritant shell gas. There was conjunctivitis, but the absence of skin burns is specifically recorded in the clinical history, and none were present at autopsy. The lesions of the upper respiratory passages appear to have been fairly characteristic of mustard gas, although the necrosis was less extreme than in many of the cases and not more severe than may occur in the influenzal cases which developed independently of previous gassing. The pulmonary lesions were those of an influenzal pneumonia, with hemorrhagic edema and typical bronchiolitis. There were also localized suppurative lesions, probably associated with a secondary *staphylococcus aureus* infection. There were interesting early reparative changes in bronchi and lung.

CASE 68.—H. A., 3131135, Pvt., Co. G, 109th Inf. Died, October 15, 1918, 7 p. m., at Base Hospital No. 18. Autopsy No. 143. Autopsy, October 16, 16 hours after death, by Maj. C. B. Farr, M. C.

Clinical data.—Gassed on October 5, 1918. Exposed to yellow cross, green cross, and blue cross shells (1,000 77 and 105 mm. shell). Admitted to Base Hospital No. 18 on October 8 with severe conjunctivitis and cough. Developed cyanosis and signs of consolidation at base of left lung. Leucocytes 9200. October 14, sputum culture negative or pneumococcus. There are many Gram-negative cocci.

Anatomical diagnosis.—Second degree burns about the eyes, and inside of nose, nostrils, mouth, and chin. Acute laryngitis, tracheitis, and bronchitis. Coalescing bronchopneumonia. Emphysema. Subpleural emphysema, right middle lobe. Fibrinous pleurisy. Fatty infiltration of liver.

External appearance.—The eyelids, periorbital skin, and adjoining areas of the nose, as well as the nares, left angle of the mouth, and folds of the chin are of a rough, dull red color, and covered by yellow crusts. There are numerous areas of localized desquamation of the skin.

Gross Findings.—*Pleural cavities*: There are fibrinous adhesions. *Heart* normal. *Left lung* is voluminous. The surface of the visceral pleura dotted and rough posteriorly, with tags of fibrin. The lower lobe is firm and airless. On section, the tissue is friable, the excised portions sink in water. The cut surface shows innumerable pinhead to pea sized firm yellowish-red areas surrounded by depressed purplish tissue. There is a moderate amount of moisture present. The upper lobe in the posterior portion is similar to the lower lobe. The anterior portion is soft, cottony, and on section, pale pink. *Right lung*: In the upper and lower lobes is similar to the left. The middle lobe is soft and cottony, except for a small tongue posteriorly, which is firm. There is slight subpleural emphysema. The general surface of the solid portion of the left, as well as the right lung, is rough, due to projections beneath the pleura of numerous small yellowish nodules. *Organs of neck*: The mucosa of the *pharynx* is pale. Tonsils are small. No lesions noted. *Epiglottis* and *larynx* slightly pinker than normal. The trachea in the lower portion, shows a thin whitish film, with pink strips corresponding to the areas between the rings. The larger bronchi are of a deep red color, show submucous hemorrhages and intense redness in general. The bronchi and the lower trachea contain gummy blood-tinged fluid.

Alimentary tract.—*Stomach, large and small intestine:* On external examination apparently normal. *Liver* shows moderate fat infiltration. Remaining organs show no significant lesions.

Microscopic examination.—*Trachea:* There is intense hemorrhagic necrosis which extends to the smooth muscle bundles overlying the mucous glands. There are very few leucocyte in the necrotic zone. The superficial epithelium, as well as that of the ducts of the mucous glands, is destroyed in its entirety, so that there is no trace of regenerative activity. Beneath the zone of necrosis, the vessels are engorged with blood. There is some fibroblastic growth, individual cells penetrating the overlying dead tissue. The mucous glands are preserved, their lumina choked with mucous secretion, and their stroma infiltrated with lymphoid and plasma cells. There is sequestration of the necrotic zone from the living tissue, although the line of demarcation is distinct. *Lung:* There are only two blocks of tissue but these show very varied lesions. There are widespread areas of loose consolidation, the composition of the exudate differing in different alveoli. The leucocytes are chiefly polymorphonuclear and are well preserved. There is a variable amount of fibrin, sometimes in the form of dense plugs, sometimes as a delicate network. Red blood cells are abundant and there are hemorrhagic areas with actual necrosis of the alveolar framework. The capillaries are engorged. The alveolar cells are frequently desquamated, but there is no epithelial proliferation. There is no hyaline necrosis of the infundibular walls. The atrial epithelium is desquamated and their lumina filled with pus. In the second block of lung, the bronchial lesions are most interesting. The wall of the bronchus is formed by a clean, highly vascular granulation tissue devoid of epithelium, and in many places infiltrated with hemorrhage. The wandering cells are almost exclusively of the mononuclear type, the majority being plasma cells. There is dense fibrinous exudate into the surrounding alveoli, and a diffuse pneumonia, poor in cells, and of the hemorrhagic edema type. Some of the atria in this block show hyaline necrosis of their walls. A well stained safranin preparation shows practically no bacteria aside from occasional plump Gram-positive rods.

NOTE.—Gas poisoning of ten days' duration with a history of exposure to mixed bombardment. The cutaneous and ocular lesions are characteristic of mustard gas. The necrosis of the respiratory tract was very deep and the destruction of the duct epithelium as well as the superficial layer accounts for the absence of regeneration. The pulmonary lesions were those of an influenzal pneumonia in all respects and the case illustrates the difficulty in differential diagnosis.

CASE 69.—C. I., 3509356, Pvt., Co. C, 20th Bat. Died, November 16, 1918, 4 a. m., at Base Hospital No. 87. Autopsy, six hours after death, by Lieut. H. H. Robinson, M. C.

Clinical data.—Said to have been gassed on November 5, 1918, but reports based on examination of Chemical Warfare Service records gives date of gassing as October 13; 2,000 77 and 105 mm. mustard shell in attack. Chief symptoms, sore throat and dyspnea.

Summary of anatomical findings.—Conjunctivæ rough and sticky. Scaly desquamation of right side of scrotum. No crusts.

Gross findings.—*Respiratory tract:* Deep injection of tracheal and bronchial mucosa, with flakes of necrotic membrane. Crumbly exudate in lumen. *Left lung:* Is light pink in color, voluminous, and emphysematous. The base of the upper lobe is studded with pinhead size abscesses surrounding bronchi. *Right lung:* Shows some areas of consolidation in the right upper lobe. Diffuse bronchopneumonia, with necrosis in right lower lobe.

Microscopic examination.—*Trachea:* The epithelium is missing. There is no exudate on the surface. Wall of the trachea is composed of granulation tissue, elsewhere infiltrated with wandering cells, chiefly small mononuclears. In places this is surmounted by wavy delicate membrane, possibly the remains of the original membrana propria. There is no marked hyperemia. *Lungs:* Four blocks were examined, (a) shows diffuse pneumonic consolidation with definite abscesses, (b and c) show larger abscesses surrounded by hemorrhage and edema, (d) shows marked emphysematous dilatation of the atria, peribronchiolitis, irregular areas of edema and edema of the interlobular septa.

NOTE.—Mustard-gas case of probably 11 days' duration. The cutaneous and ocular lesions were very slight. Neither the tracheal nor bronchial lesions

were very characteristic. There was extensive bronchopneumonia with abscesses, not of the influenzal type, and apparently limited to the right lower lobe.

CASE 70.—W. K., 48564, Pvt., Co. M., 18th Inf. Died, October 12, 1918, Gas Hospital, Julvécourt. Autopsy No. 51. Autopsy, October 12, — hours after death, by Capt. James F. Coupal, M. C.

Clinical data.—Exposed to mustard gas on October 1, 1918, passing over an area previously shelled.

Anatomical diagnosis.—Superficial burns of body (mustard gas). Bronchopneumonia. Ulcerative tracheitis. Acute fibrinous pleurisy.

External appearance.—Superficial burns of eyelids, conjunctivæ, corneæ, bends of elbows, serotum, and buttocks. Scattered areas of brown pigmentation about elbows.

Gross findings.—*Pleural cavities:* Fresh fibrinous adhesions over both lungs. No fluid. *Heart:* Right heart dilated, otherwise normal. *Left lung:* Is voluminous. On section, scattered areas of consolidation with edema in the intervening portion and emphysema anteriorly. The small bronchi are filled with pus. *Right lung:* Presents the same picture. *Organs of neck:* Base of tongue and fauces are markedly injected. *Trachea and bronchi* are denuded of mucous membrane and contain purulent exudate. *Alimentary tract* not recorded. The remaining organs show nothing of interest.

Microscopic examination.—*Trachea:* The epithelium is absent. There is no pseudo-membrane. Submucous layers are somewhat edematous and infiltrated with polymorphonuclears and mononuclear leucocytes. Capillaries are congested. Some of the mucous glands contain normal epithelial cells; others show mucous secretion, are surrounded by lymphocytes and other inflammatory cells. The large bronchi are the same as above. Clumps of bacteria are present in the superficial submucous layers. *Lungs:* The smaller bronchi contain pus cells and granular detritus. Submucous layers are infiltrated with polymorphonuclear leucocytes and a few red blood cells. There is marked peribronchial congestion. There is an area of typical lobular pneumonia with clumps of cocci distributed amongst the leucocytes in the alveoli. The unconsolidated portion of this section shows emphysema. The remaining organs show nothing of interest.

NOTE.—Mustard-gas case of 11 days' duration. There were no special features except the absence of reparative changes of the epithelium of the bronchi of the lung.

CASE 71.—H. G., 113263, rank ?, Co. B, 150th M. G. Bat. Died, April 1, 1918, at Base Hospital No. 18. Autopsy No. 55. Autopsy, four hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Gassed on March 21, 1918, while attending to mules back of the trenches. Four hours later developed severe cough and conjunctivitis. On the following day, burns about the penis. On admission, marked conjunctivitis, throat deeply injected. Right middle lobe, dull to percussion, tubular breathing and râles. March 28, both lungs involved, bronchitis, laryngitis, and delirium. April 1, unconsciousness, cyanotic. Temperature 101° to 105°.

Anatomical diagnosis.—First degree healing burns of skin, conjunctivæ, posterior pharynx, upper esophagus. Diffuse patchy pigmentation of skin. Acute diphtheritic esophagitis, laryngitis, bronchitis, and tracheitis. Extensive bronchopneumonia. Acute fibrinous pleurisy. Pulmonary edema. Obsolete tuberculosis of peribronchial lymph nodes. Dilatation of right auricle.

External appearance.—There are extensive areas of desquamation of the skin over inner surfaces of the thighs. Areas showing innumerable tiny vesicles over the upper chest, upper forearms, and axillæ. There are good-sized vesicles on the backs of the hands, and on the back of the left hand there is a large bulla, 4 cm. in diameter, containing a considerable amount of clear fluid. There are areas of practically healed superficial ulceration about both knees, wrists, bend of right elbow, right buttock, serotum, penis, and lips. These are, in places, healed completely, and in places covered by brown scabs. The skin everywhere shows a striking muddy pigmentation. In addition, there are large irregular dark brown areas of pigmentation, in places, associated with the skin lesions mentioned above, in places, especially over the abdomen unassociated with any skin lesions. The distal portion of the

extremities quite free from the intenser pigmentation. *Eyes*: Eyelids puffy, lids glued together by caked exudate. Conjunctivæ swollen, injected; there are small hemorrhages. Both corneæ everywhere transparent. Pupils are about equal, 3 mm. *Nose*: No abnormalities. *Mouth*: A few areas of superficial ulceration with scab formation about the lips.

Gross findings.—*Pleural cavities* are free of fluid and adhesions. *Heart*: Normal, in position and shows no significant lesions. *Right lung*: Weighs 900 grams. *Left lung*: Weighs 710 grams. All lobes are voluminous, cushiony, soggy. Both upper and lower contain solid areas. The pleura in general is thin and glistening, but over the posterior surfaces of the right upper and lower and median anterior surface of the upper it is somewhat glazed, and there is a small amount of fibrinous exudate which peels readily. There is also a moderate amount of fibrinous exudate between the lobes, and here and posteriorly there is a moderate number of red subpleural hemorrhages. *Organs of neck*: The glands of the neck and mediastinum moderately enlarged, pulpy, and injected. *Thyroid* of good size, tissue pale, acini filled with colloid. *Trachea*: The lower one-third shows necrosis of the epithelium, with ulceration. The process extends into the submucosa. There is a considerable amount of necrotic and fibrinous membrane, below which the tissue is greatly injected and somewhat swollen. In the upper one-half of the trachea there is some necrosis of the epithelium. In the *larynx* the epithelium is practically necrotic, below it the tissue is greatly injected. The dead epithelium strips readily. In places the necrotic epithelium is associated with considerable coherent fibrinous and fibrinopurulent exudate. This is especially true of the true vocal cords. There is an extension of the process into the esophagus and the base of the tongue. *Tonsils*: In part are scarred, in part pulpy. A few of the crypts contain dry, yellow, opaque material. *Alimentary tract*: No abnormalities, except that the lymphoid tissue is slightly more prominent than normal, especially in the lower ileum. The mesenteric glands are small and pulpy. The remaining organs show nothing of interest.

Microscopic examination.—*Trachea*: No specimens. *Lungs*: Only a single section showing massive alveolar edema, no fibrin. *Liver, spleen, and kidneys*: Show no significant lesions.

NOTE.—Typical mustard-gas case of 11 days' duration, but the histological material was inadequate for study.

CASE 72.—V. P. T., 1588715, Pvt., Co. G, 30th Inf. Died, August 28th at 6 p. m., at Base Hospital No. 27. Autopsy No. 42, performed 1 hour after death, by Capt. H. H. Permar, M. C.

Clinical data.—August 10, admitted to Field Hospital No. 7, suffering from mustard-gas contact and inhalation. August 12, admitted to Base Hospital No. 27. Severe burns of eyes back, thighs, legs, and arms. Pain in throat, cough and tightness in chest. *Heart* negative. Many sonorous râles over both sides of chest. Extensive exudate in throat from burns.

Anatomical diagnosis.—Brown pigmentation of skin of body; third-degree burns on buttocks, hips, and calves of legs, conjunctivitis, acute healing; tracheitis, acute healing; bronchitis, acute purulent; bilateral; bronchopneumonia, early; bilateral; pulmonary emphysema; atelectasis of left upper lobe; acute fibrinous pleurisy; old pleural adhesions, bilateral; hydrothorax, bilateral; cardiac dilatation, right side; acute lymphadenitis, and tuberculosis of peribronchial lymph nodes; congestion and cloudy swelling of liver and kidneys.

Microscopic examination.—(Four blocks taken for examination.) Marked thickening of the bronchi, the walls of which are composed of opaque whitish tissue, 2 to 3 mm. in thickness, is noted in the fragment of preserved lung tissue. (a) The largest bronchus in the section is almost filled with purulent exudate, in which are masses of bacteria, and which toward the periphery has the character of a partially adherent fibrinopurulent membrane. Over roughly one-half of the circumference the epithelium is entirely defective; over the remainder there is a loosely attached strip of laminated, pale nonciliated cells, several rows in depth. The individual epithelial cells, especially those near the surface, are vacuolated, their nuclei shrunken and distorted, and there are many leucocytes passing between them. In one place, the epithelium is lifted up by a bleblike accumulation of fluid, appearing as a shreddy coagulum in the section. The bronchial wall is at least 2 mm. thick, and is composed of a fairly vascular granulation tissue, infiltrated near the surface with polymorphonuclears, and in its deeper portion with lymphoid and plasma cells. The mucous glands are partly preserved but many of the acini are atrophic. The cartilages are small in comparison to the size of

the bronchus; the matrix stains with eosin, and the nuclei appear degenerated. Small nerve trunks, embedded in the granulation tissue, show a proliferation of the endo- and perineurium, and are invaded by wandering cells. Another bronchus of about the same caliber shows similar changes, but there is less inflammation, and the reinvestment with metaplastic epithelium is more extensive. It is interesting that the new epithelium shows vacuolization of the epithelial cells, like that seen in the original burns. At the same time there are numerous mitotic figures. The arteries are surrounded by a broad zone of edematous granulation tissue. The lung tissue in the section shows a patchy edema, with some exfoliation of epithelial cells. (b) The section includes several bronchi of medium size. One of these is completely occluded with a fibrinous plug, loosely infiltrated with wandering cells; another is filled with pus and bacteria. In both, epithelium is entirely destroyed and the bronchial wall replaced by thick granulation tissue. The parenchyma shows emphysematous vesicles interposed between small areas of collapse and lobular pneumonia. An interesting feature is a marked stenosis of some of the smallest bronchi, the lumen of which is reduced to an irregular split, and the wall proportionately thickened. (c) The changes in the larger bronchi are like those described, some being completely reinvested with squamous epithelium, others still showing a severe diphtheritic inflammation with adherent laminated fibrinous membrane. The lung tissue is the seat of a hemorrhagic and fibrinous edema, which in the neighborhood of the bronchi is becoming organized by the ingrowth of fibroblasts. The alveolar septa are thick and infiltrated with wandering cells, chiefly lymphoid. There is an obliterating bronchiolitis in some areas. This is not associated with organization of the bronchial exudate, the lumen being free, and the epithelium normally ciliated. It appears to be caused rather by the contraction of the granulation tissue in the wall of the bronchiole. (d) The bronchial changes are like those in the previously described sections. The lung tissue itself shows an extensive edema. Many of the alveoli also are packed with well-preserved desquamated epithelial cells, amongst which are large multinucleated forms.

NOTE.—A case of severe mustard-gas poisoning, dying 11 days after exposure with typical cutaneous and respiratory lesions. The permanent changes which resulted from the intense bronchial injury are already indicated, and cicatrization and repair were seen, together with the destructive effects of the original injury.

CASE 73.—W. H. T., 2414146, Pvt., Hdqrs. Co., 312th Inf. Died, November 1, 1918, at 5.10 p. m., at Base Hospital No. 41. Autopsy No. 41, performed two hours after death, by Lieut. L. G. Gage, M. C.

Clinical data.—Gassed with mustard shell gas on October 21. Admitted to Mobile Hospital No. 4 on October 25, with diagnosis of mustard-gas burns, multiple shrapnel wounds, and fracture of right fibula. October 27, admitted to Base Hospital No. 41. Diffuse bronchitis.

Anatomical diagnosis.—Mustard-gas burns of skin; acute conjunctivitis; membranous laryngitis, tracheitis and bronchitis; acute bronchopneumonia; anomalous left kidney; multiple shrapnel wounds.

External appearance.—There is a dermatitis of eyelids, corner of mouth, lips, and nostrils. The epithelium is sloughing on inner surface of the thighs. The prepuce and glans penis are very edematous. There are multiple superficial shrapnel wounds over both legs. There is a penetrating wound just to the outer side of the right tibia.

Gross findings.—*Left lung:* Weighs 720 grams. It does not collapse readily after removal. The lower posterior portion of the upper lobe and the lower lobe are dark blue in color, firm in consistence. On section, the upper lobe has a pink color, but scattered through it are small dark red areas which surround the bronchioles. These contain a fibrinomucoid secretion. The main bronchus contains a fibrinous membrane beneath which the mucosa is congested, hemorrhagic and eroded. The lower lobe is solid, of beefy consistence, and dark red in color. The bronchioles are surrounded by patches of grayish consolidation. *Right lung:* Weighs 920 grams and presents lesions similar in character to those on the left side. (Additional note dictated from preserved Army Medical Museum specimen.) The specimen includes half of upper and lower lobes of right lung. The pleura is covered by a delicate fibrinous exudate. The surface of the lung is smooth, and the lobular structure obliterated.

On section, the lower portion of the upper lobe, and the entire lower are solid, airless, dark red. The large bronchi show erosions of the mucosa with grayish membranous deposits. The small bronchi are more or less filled with yellow fibrinopurulent exudate. *Larynx* is covered with fibrinous exudate under which the mucous membrane is congested, hemorrhagic, and eroded. *Trachea* shows a similar membrane. The congestion increases toward the bifurcation. *Gastrointestinal tract*: Not recorded. The remaining viscera show no lesions of special interest.

Bacteriological examination.—Culture from lung (post-mortem) hemolytic streptococcus.

Microscopic examination.—*Large bronchus*: The epithelium is in large part preserved, and is normally ciliated. Where exfoliation has occurred, this appears to have been post-mortal. The submucosa is not markedly edematous and there is no acute inflammatory infiltration. The capillaries are engorged, and there are small hemorrhages. The picture does not correspond closely to the description of the gross lesions. *Lungs*: The picture is an unusual one. The bronchioles and infundibula are filled with masses of bacteria and mucus, with a variable number of leucocytes. The epithelium in most of them is wholly destroyed. The parenchyma shows practically no aerated alveoli, the alveolar spaces being filled with homogeneous coagulum, or in places a fibrinous plug, in which are numbers of red cells and alveolar epithelium. The hemorrhage in some portions of the sections is very abundant. Into the plugs are seen growing pale fibroblasts, but the organization is very early and limited to comparatively few alveoli. The exudate is practically free from leucocytes, but there is an increased number in the alveolar septa.

NOTE.—The duration of life after gassing in this case was eleven days. The skin burns bore out the clinical diagnosis of mustard-gas poisoning, but the respiratory lesions were less clear-cut. A membranous tracheobronchitis was described in the gross, but sections of a large bronchus failed to confirm this. The pulmonary lesions conformed to the acute influenzal type, with abundant hemorrhagic edema and an aplastic exudate. It is to be noted that the case occurred during the period when the influenzal epidemic was at its height. The case illustrates the difficulty in differential diagnosis.

CASE 74.—T. B., 124463, Pvt., Labor Corps, 204 Emp. Co. Died, November 1, 1918, at 4.40 a. m., at Base Hospital No. 2. Autopsy, five hours after death, by Lieut. J. H. Mueller, San. Corps.

Clinical data.—October 20, admitted to No. 47 Casualty Clearing Station. Irritant shell gas poisoning. October 22, admitted to Base Hospital No. 2. Nauseated; pain in abdomen; eyes and throat irritated and sore. Temperature 104.4°. Pulse 110. October 23, conjunctivitis; pharyngitis; chest clear; heart normal; pulse 80; abdomen, slight tenderness. October 24, temperature 104. Respirations normal; very drowsy; chest shows a few coarse râles in right axilla and under right scapula; coughing. No diarrhea; nauseated during night. Sputum smear shows mixed flora, Gram-positive diplococci, bacilli, etc. Plate staphylococcus, streptococcus viridans. Blood count, white blood cells, 9,150. Polymorphonuclears, 84 per cent. Small lymphocytes, 10 per cent. Large lymphocytes, 5 per cent. Transitionals, 1 per cent. October 25, temperature 103°. Small patch of relative dullness over right back in posterior axillary line near axilla. Bronchovesicular breathing and a few râles in this area. Urine, heavy trace of albumin; many finely granular casts. No cells. October 26, temperature 102°. Chest shows very slight change. Slight impairment at bases, also over right subscapular region; moist râles in these areas. Cyanotic, labored respiration; complains of pain in chest and lower lumbar region. October 30, condition worse, jaundice; many fine and coarse râles over entire chest; suppressed breathing. Blood culture sterile. October 31, marked jaundice; gasping; pulse rapid and weak. November 1, died at 4.40 a. m.

Anatomical diagnosis.—Acute purulent tracheobronchitis; bronchopneumonia; localized empyema; acute perihepatitis; icterus; poisoning by inhalation of irritant gas.

External appearance.—Moderate emaciation. Fairly marked jaundice evident over the whole cutaneous surfaces and particularly marked in the sclerae. There is an erythematous rash over the back. No other cutaneous lesions.

Gross findings.—*Pleural Cavities*: Free from fluid. *Left lung*: Lightly adherent along its posterior surface by thick fibrinous adhesions. The pleura is smooth except for this

area, which is slightly dulled. The bronchi contain thick bloody pus, and their surfaces are red and eroded. The larger vessels are normal. On section, the upper lobe is practically normal, being air containing throughout except for some small areas of bronchopneumonia at the base. The lower lobe is largely affected; it is very edematous and bloody. The consolidation is lobular, the consolidated areas being in places hemorrhagic, in others flesh-colored and translucent. The bronchi are not noticeably prominent. *Right lung:* Shows a rather more extensive exudate over the lower lobe. In addition, the lower portion of the upper lobe, on its anterior surface, and also on its mesial surface, shows a thick yellow exudate of purulent material. On section, all lobes are heavily involved in a lobular consolidation resembling that of the opposite lung. In one place in the lower lobe there are a number of small grayish-white areas, cutting with a fairly flat surface, perhaps slightly projecting, each about 0.5 cm. in diameter. These are dry, opaque, and granular in distinction to the surrounding lung. Bronchi show the same bloody exudate as on the left side, the smaller bronchioles not being prominent. *Organs of neck.*—*Trachea:* Shows an intense congestion with deep ulceration of the entire mucosa; glottis is similarly affected. *Heart* normal. *Liver:* Bile passages patent. *Gall bladder* contains a small amount of dark green fluid bile. There are no stones. Over the portion of the liver adjoining the diaphragm, there are partly organized fibrinous adhesions uniting the two. *Stomach and intestines:* Normal except for slight congestion of the lower portion of the ileum. Remaining viscera show no significant lesions.

Microscopic examination.—*Trachea and large bronchus:* No sections. *Lungs:* Four blocks showing similar pictures. No larger bronchi are included in the sections. The bronchioles and infundibula contain dense plugs of fibrinopurulent exudate; the epithelium shows in places early regeneration, and is frequently in the form of a single flat layer. Elsewhere there is an intense confluent hemorrhagic pneumonia. The exudate in some of the air spaces is composed predominantly of polymorphonuclears, pycnotic and distended with bluish granular material, which in Gram-stained sections are disclosed as a variety of Gram-positive and negative bacteria. Many of the Gram-negative organisms are cocci. There is practically no fibrin in the exudate. There are several areas of necrosis in which the alveolar walls are involved. In some areas there is profuse fresh hemorrhage, completely filling the alveoli. Mixed with the blood cells are pigment containing alveolar cells. Near the pleura there is active epithelial proliferation, new cells investing the alveolar wall and covering over the plugs of exudate. (See fig. 26.) *Spleen, kidney, and myocardium:* No significant changes.

NOTE.—Death 12 days after definite exposure to irritant shell gas. No cutaneous lesions, but there was conjunctivitis and marked icterus. There was an ulcerative tracheobronchitis, without definite membrane formation. The lungs showed a hemorrhagic lobular pneumonia with edema, of the influenzal type, with epithelial proliferation.

It is not possible from the data at hand to make a definite diagnosis of mustard-gas poisoning, nor indeed, aside from the clinical history, is there any convincing evidence of previous gassing. The lesions present might all be attributed to an influenzal infection with pneumonia.

CASE 75.—T. M., 561720 (rank not given), Hdqrs. Co., 59th Inf. Died, August 18, 1918, at 8.25 a. m., at Base Hospital No. 17. Autopsy, performed ? hours after death. (Name of pathologist not stated.)

Clinical data.—Gassed on August 8. No further details available. The records include no other fatalities from gassing in the same company on or about this date, but soldiers from Companies D and H of the 59th Infantry were gassed on August 5 and 6 with yellow, blue, and green cross shells. It is possible that T. M. was exposed on the same date. August 8, admitted to Field Hospital No. 28. Exhausted. Blisters on scalp. Bath. Blisters dressed. Transferred to Evacuation Hospital No. 5, and on August 9, to Base Hospital No. 17. Cyanosis, marked dyspnea, air hunger, tachycardia, heaving displaced apex. Lungs showed typical physical signs of edema. August 10, cyanosis and dyspnea not improved. Pulse rapid and thready but regular. No dullness, but large and small râles with prolonged blow at end of each respiration. Oxygen administered. Died on August 18. Autopsy protocol not received.

The following note was dictated from the preserved Army Medical Museum specimen, which consists of the neck organs, with left lung attached, in formalin:

The base of the tongue and pharynx are normal. The inferior surface of the epiglottis and false cords of the larynx are covered by grayish flakes of exudate which are easily detached. The trachea is pale throughout. The lining is a little rough and granular, and largely denuded of mucosa. Beginning about the middle, however, there are islands of a grayish white adherent membrane which resembles patches of regenerated epithelium rather than a diphtheritic exudate. The large bronchi, especially after the first division, still contain much fibrinopurulent exudate. On section, both lobes of the left lung are air containing except for scattered patches of edema and partial atelectasis. The bronchi on cross section have opaque thick walls; many of them are completely occluded by membrane or exudate. The anterior portion of the upper lobe shows a group of small bronchiectases lined with necrotic material.

Microscopic examination.—*Trachea:* The surface is in part denuded of epithelium, in part covered with islands of stratified squamous cells, often six or more layers deep. The ulcerated regions are surmounted by a loose exudate composed of red blood cells, polymorphonuclears and detritus. There is very little fibrin and no formed pseudomembrane. The mucous ducts show the usual epithelial proliferation. The subepithelial tissue is the seat of a dense inflammatory infiltration, both polymorphonuclears and of lymphoid cells. There are very dense accumulations of lymphocytes about the otherwise normal mucous glands. *Lungs:* Section includes a group of medium-sized bronchi greatly distended with purulent exudate. The epithelium and glands are destroyed but the cartilages about the larger branches are still intact. The alveoli about these bronchiectases are compressed and the septa thickened and infiltrated. Some of them contain fibrinous exudate, others fresh blood. In many, organization is in progress. The connective tissue about the bronchi and blood vessels is edematous and contains many fibroblasts. (Fig. 33.) A second block of lung shows an acute suppurative bronchitis with moderate dilatation and inflammatory thickening of bronchial wall, leading in one place to necrosis of the bronchial cartilage. In many places the alveolar septa are condensed and infiltrated with dense collections of leucocytes, largely mononuclear. Practically no exudate in alveolar spaces.

NOTE.—An incompletely studied case; death 10 to 12 days after gassing. The nature of the gas to which the soldier had been exposed is uncertain, but the clinical history suggests an admixture of suffocative gas in addition to the vesicant. The regenerative changes in the tracheal epithelium are of interest.

CASE 76. T. M., 2849228, Pvt., Co. H, 359th Inf. Died, October 11, 1918, at 2 a. m., at Base Hospital No. 45. Autopsy No. 52. Autopsy, October 12, 31 hours after death, by Capt. Jean Oliver, M. C.

Clinical data.—Gassed on September 28, 1918. The following extract is taken from field card: "Was sleeping in dugout when gassed, also got some gas after leaving dugout, burned eyes, throat, and lungs; got sick at stomach and vomited, coughed good deal since. Physical examination: Eyes red, lids swollen, lachrymation and photophobia. Coughing some and spitting up mucopurulent sputum. Hoarse. Diagnosis: Mustard and diphsogene." On admission to Base Hospital No. 45 on October 5 complained of intense pain in throat and on swallowing. Face cyanotic, pulse rapid, temperature 102°. Dullness over right lower lobe. Fine crepitant râles.

Anatomical diagnosis.—Mustard-gas burns, on lips, eyes, nose, and over scrotum. Diphtheritic laryngitis, bronchitis, and tracheitis. Diffuse bronchopneumonia of all lobes of both lungs.

Following abstract was dictated upon the receipt of specimens at the pathological laboratory, Experimental Gas Field:

The posterior wall of the pharynx shows a superficial necrosis with a grayish membrane. The epiglottis and trachea present a worm-eaten appearance (erosions) and are covered in places with a sandy grayish deposit. The bronchi, larger branches, show intense purplish-red discoloration. There are patches of flaky exudate on the surface. After the second or third branching, the mucous membrane becomes smooth. The lumina contain very little exudate. The left lung is moderately heavy and voluminous. There is fresh fibrin in spots

over the posterior portion of the lower lobe. The color is mottled bluish purple. On section is generally air-containing. There are, however, a few shotty elevated areas of consolidation. These are not over 1 cm. in size. The bronchi are surrounded by a zone of hemorrhage 2 to 3 mm. broad. Elsewhere the lung tissue presents a marbled appearance because of irregular, uniform, darker areas, slightly prominent above the surface, which are partly consolidated. The lower lobe is very dark in color and poorly aerated. It contains a number of small shotty pneumonic patches. The right lung shows fresh fibrin over all lobes. On section there are numerous areas of lobular pneumonia, rather discrete and small for the most part, and distributed throughout all lobes.



FIG. 33.—Case 75. Death probably 10–12 days after exposure to mixed gases. Bronchiectases filled with purulent exudate. Peribronchial and periarterial edema and beginning fibrosis

Microscopic examination.—*Trachea:* The mucous membrane is of the stratified squamous type. In places it is partly exfoliated and there is false membrane. The sub-mucous tissue shows engorged vessels, edema, and a slight infiltration with mononuclear cells, large and small. This is especially marked about the mucous glands. A few bacteria are seen on the surface of the mucous membrane. *Medium-sized bronchus:* In places there are patches of adherent membrane composed of swollen reticulated fibrin. The wall of the bronchus is completely necrotic and there is no beginning of regeneration. Beneath the necrotic lining there is edematous tissue, poor in cells. About the bronchus there is the usual zone of intense hemorrhage. *Lungs:* The small bronchi show desquamated columnar epithelium. The lumina are filled with polymorphonuclear leucocytes. The walls are

congested and acutely inflamed. The parenchyma is the seat of a bronchopneumonia of wide but patchy distribution. The exudate varies in its contents of edematous fluid, red-blood cells, polymorphonuclear leucocytes and fibrin. Usually there are well-defined areas in which one or more of these elements predominates. Bacteria are numerous both in the bronchi and the pneumonic areas, almost extensively Gram-positive cocci, some in large masses, others in swollen groups and chains. It is evident from the naked-eye inspection of the lung section that many of the bronchi are both dilated and thickened. The dilatation is shown by the flattening of the adjacent alveoli. The thickening is produced by edema and peribronchial organization of the connective tissue. The periarterial tissue is also thickened. *Liver, spleen, kidneys, pancreas, and intestines* show no significant lesions.

NOTE.—Mustard-gas poisoning; death on the thirteenth day after exposure. There was no anatomical reason to support the clinical diagnosis of mustard-gas and diphosgene poisoning, the lesions differing in no respects from other mustard-gas cases. It must be said, however, that it would probably not be possible to recognize the effects of an admixture of suffocant gas after this time had elapsed. The trachea and large bronchi showed well-established epithelial regeneration, and it is possible that the necrosis was superficial. The smaller bronchi, on the other hand, showed extensive necrosis with beginning fibrosis of their walls, and dilatation. There was the usual peribronchitis with fresh hemorrhagic pneumonia. The consolidation was distinctly in relation to the bronchi.

CASE 77.—J. C., 2706880, Pvt., Co. H, 136th M. G. Bat. Died, October 28, 1918, 3.40 a. m., Base Hospital No. 45. Autopsy No. A 18-67. Autopsy, 10 hours after death, by Lieut. Perry J. Manheims, M. C.

Clinical data.—Gassed about 6 a. m. October 14, 1918, in action, 2,000 150-mm. shells. Clinical diagnosis: Bronchopneumonia following inhalation of mustard gas.

Anatomical diagnosis.—Multiple superficial mustard-gas burns. Diphtheritic tracheo-bronchitis. Bronchopneumonia. Hemorrhagic erosions of stomach.

External appearance.—Superficial burns about mouth, nose, and right cheek, covered with thick brownish red scabs. Skin on inner surface of both thighs shows small dry blisters, confluent in places, extending from 3 cm. above knees to level with serotum. Few dry scabs on under surface of serotum and prepuce. Skin about the axillæ shows the same condition as the thighs.

Gross findings.—*Respiratory organs:* Sent to Chemical Warfare Service. *Stomach:* Shows a few hemorrhagic erosions. The remaining organs show no significant lesions.

The following note on the gross appearance of the respiratory organs was made upon the receipt of the specimens at the pathological laboratory, experimental gas field:

The posterior wall of the *pharynx* shows necrosis and is covered with patches of gray membrane. The *tonsils* are smaller than usual, with deep crypts containing cheesy plugs. The inferior surface of the *epiglottis*, *voal cords*, and *trachea* show complete necrosis of the mucous membrane, which is replaced by a soft slough. The *bronchi* are filled with a thin purulent fluid. The mucosa is necrotic and desquamated. There is no definite membrane. *Left lung:* Weighs 525 grams. The pleura is smooth. Firm nodular areas can be felt through the upper lobe. On sections these correspond to elevated 1 to 2 mm. sized areas of consolidation scattered about the bronchi. The latter are filled with pus. There is the same appearance in the lower lobe. The bronchi seem rather thick and project above the surface. *Right lung:* Weighs 700 grams. There are large areas which show a grayish-blue color through the pleura, which are quite soft and have lost their elasticity. These areas occupy the posterior two-thirds of the upper and middle lobes and the upper and posterior parts of the lower lobe. On section, the lung tissue is broken down, exuding a large amount of thin bloody fluid. There is no gangrenous odor. The anterior portion of the lobes contain numerous small greenish areas of consolidation, apparently peribronchial.

Microscopic examination.—*Skin:* Illustrates the late effect of a mild burn. There is hyperkeratosis; many of the epidermal cells show pyenotic nuclei and contain vacuoles, and the papillary layer of the corium shows edema. There are occasional pigment cells, but no

marked increase. Inflammatory changes are absent. *Primary bronchus:* The membrane has been cleared away. The surface is formed by continuous membrana propria which is uncovered by epithelium. Immediately beneath it are fairly dense accumulations of leucocytes (pyenotic). The submucous tissue is very loose and edematous. Many of the venules contain dense hyaline thrombi, some of which are being covered with endothelium. In the deeper submucosa there is a proliferation of fibroblasts. The mucous glands are in active secretion and are not abnormal. The section includes no submucous ducts. *Lungs:* The most interesting changes are found in some of the bronchi, which, with the low power, are slightly thick walled, and under the high magnification show clearly an active hyperplastic growth with numerous plasma cells. The bronchi are relined with flattened epithelium. The parenchyma is the seat of irregular patches of bronchopneumonia, some of which are in definite relation to bronchi which are filled with purulent exudate. There are no special features to the exudate. In a few areas where fibrin is abundant organization is in progress. Bacteria are difficult to demonstrate. A few Gram-positive cocci are found in the bronchial exudate. Cultures at autopsy from lung show hemolytic streptococcus.

NOTE.—Mustard-gas poisoning; death 14 days after exposure. Characteristic burns. Atria and bronchi showed a cleaning up of the tissue with subsidence of the acute inflammatory process, but no epithelial regeneration. The small bronchi were already thickened and dilated. Some of them were relined with new epithelium, though incompletely. There was still an acute lobular pneumonia distributed about the infected atria. The usual organization of the exudate was in progress in certain places. The gangrenous areas in the right lung were, unfortunately, not examined histologically.

CASE 78.—P. C., 61723, Pvt., Co. 2, 101 Inf. Died, June 14, 1918, at Base Hospital No. 18. Autopsy No. 63. Autopsy, one and one-half hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Said to have been gassed with phosgene on May 31, 1918, while on raid on enemy's trenches. On return to own trenches developed cough; was carried to Field Hospital No. 103. Transferred to Base Hospital No. 18 on June 2. On admission temperature 102°, comfortable. Râles in both lower lobes. June 4, temperature 105°, moderate cyanosis, rapid respiration. Signs of bilateral bronchopneumonia, most extensive in lower lobe. Blood pressure 95/50. Heart not dilated. On June 5, temperature 105°, respiration 34, cyanosis, feeble pulse. June 6, consolidation of entire left lung. General condition better, apparent crisis. June 9, temperature again elevated. Delirium, Cheyne-Stokes; profound prostration. Irregular consolidation, right upper lobe. Stupor. Leucocytes, June 5, 13,800; June 10, 16,300; three blood cultures negative.

Anatomical diagnosis.—Acute tracheitis and bronchitis, following phosgene inhalation. Extensive bronchopneumonia, discrete and conglomerate with areas of organization. Acute bronchial lymphadenitis. Moderate fat infiltration of liver. Acute colitis. Few small healed infarcts of right kidney. Acute dilatation of right ventricle. Healed tuberculous foci of bronchial and tracheal lymph nodes.

External appearance.—*Skin* is sallow in appearance. About the right shoulder and forearm there are a number of flat, irregular, pearly white blotches in the skin, suggesting old burns. In the skin of both legs there are small excoriated areas suggesting pediculosis, also a number over the chest. At the bend of the left elbow there are a few puncture wounds. Superficial glands are palpable. *Eyes:* Pupils slightly divergent, squint. Pupils greatly dilated, 7 mm. Conjunctivæ and other mucous membranes pale. Some cyanosis of the lips. *Nose and ears:* No abnormalities. *Mouth:* Some sordes covering the lips and gums. Also a moderate amount of mucus.

Gross findings.—*Pleural cavities:* Opening the thorax, the median portions of the upper lobes almost meet in the midline. The pleural sac is free of adhesions and fluid. The heart is enlarged slightly to the right. No abnormalities in the sac. *Heart:* Weighs 290 grams. Moderate dilatation of the right ventricle. Otherwise negative. *Right lung:* Weighs 600 grams. All lobes are voluminous. The posterior and lateral portions of the upper and lower lobes soggy, solid, the median portions cushiony. The middle lobe cushiony, pink. The glands at the hilum are considerably enlarged, pulpy, somewhat edematous, pale. Some

of the glands at the hilum have small scarred gray areas, plus anthracosis. The bronchi are filled with thin, viscid yellow pus. On section of the upper lobe, the posterior and lateral one-half dull gray-red and red, solid in great part, mottled with small grayish and yellowish pinhead sized areas. The median one-half is pink, aerated. Through it there is a moderate amount of discrete and conglomerate small gray nodules, quite firm in consistence. On section of the middle lobe, the tissue crackles, is well aerated, pink; scattered throughout, there is a moderate number of discrete and conglomerate pinhead sized yellowish-gray solid areas. Some of these more firm in consistence than others. In the lateral portion of the lobe there is some grayish consolidation about these conglomerations. The lower lobe, on section, shows in the posterior and lateral portions collapsed deep red lung tissue mottled with a large number of discrete and conglomerate grayish and yellowish nodules, mostly gray with fairly firm consistence. About these conglomerations, more medially, there are discrete hemorrhages. About these medially the tissue is well aerated, pink, shows a moderate number of discrete and conglomerate solid gray areas, quite firm in consistence. In this lobe there is a little uniform consolidation and that present is found in the posterior and lateral portions of the lobe. *Left lung:* Weighs 800 grams. Both lobes voluminous, soggy, solid. The median portions, especially, show well-aerated tissue in which are felt numerous small nodules. The pleura over the lobes on this side and over the lobes on the right is thin, delicate and pale. The glands at the hilum and bronchi are similar to those on the right. On section, the upper lobe is mottled reddish and yellowish, surface presents with, here and there, areas of pink. The yellowish areas are discrete and conglomerate. The solid areas are associated with bronchial branches. The peripheral portions of greater consistence than the central portions. In places there are more firm solid areas. The dull reddish-gray areas are large consolidated patches, in places confluent. The surface is relatively dry, slightly granular, surrounding the numerous groups of yellow conglomerations mentioned above. The lower lobe, on section, shows a picture quite similar to the right lower lobe, except that the hemorrhage about the conglomerate yellow areas is much more marked. Associated on this side there is present some diffuse consolidation. The nodules, likewise, in this lobe are more numerous and of less consistence than those in the right lower lobe. *Organs of neck:* Lower tracheal and cervical glands are quite similar to the glands about the hilum. In addition some show calcified nodules. The *thyroid* is small and tissue pale. Acini contain some colloid. The *larynx* and *trachea* contain a considerable amount of viscid yellow pus. The mucosa is pale, thin, except in the lower portion of the trachea, where it is somewhat swollen and somewhat injected diffusely. *Tonsils:* Small, scarred, and crypts clean. *Alimentary tract:* Stomach is small. The walls are moderately contracted. There are a few 100 c. c. of thin bile tinged mucus in it. The duodenum and the jejunum contain bile tinged contents. The lymphoid tissue in the tract is slightly more prominent than normal. Throughout the large intestines there are large patches of injection of the mucosa with small hemorrhages. In these areas the lymphatic follicles are very prominent, and covering the mucosa there is adherent tenacious mucus. The rectum is similar in appearance. The injection here is more marked. The mesenteric glands are somewhat enlarged, pulpy, pale. *Liver:* Weighs 1,530 grams. Shows slight fat infiltration. *Kidneys* show focal scars.

Microscopic examination—Trachea: No sections. *Large bronchus:* The epithelium is continuous and very orderly in arrangement. The superficial layer is beautifully ciliated. There are occasional mitoses. Leucocytes, polymorphonuclears and mononuclears are wandering between the epithelial cells. The submucosa is not edematous nor extremely congested. There are numerous lymphoid and plasma cells but very few polynuclears. The mucous glands are in active secretion, otherwise normal. *Lungs:* There is an intense bronchiolitis and infundibulitis. The lumina are filled with pus, their epithelium is largely preserved, and in many cases regenerated, multiple-layered and nonciliated. There is an early organization of the bronchiolar exudate in places. The bronchial walls are thickened, partly by edema and inflammatory changes, and partly by new growth of connective tissue which extends into the septa of the neighboring alveoli. There is a marked peribronchitis, the alveolar exudate consisting often of dense plugs with few leucocytes. There is an early ingrowth of fibroblasts, and an epithelial proliferation. Epithelial cells are relining the alveoli and in the form of syncytial masses growing over and into the fibrin plugs. Another block shows a slightly different picture. Many of the infected atria, which have completely lost their epithelium, appear as abscesses and are surrounded by confluent areas of hemor-

rhagic and fibrinous pneumonia, in which organization, interstitial fibrosis, and regeneration of the alveolar epithelium are conspicuous features. A study of the sections stained with Gram-Weigert-safranin under the low power magnification with a binocular microscope shows in a very interesting way the distribution of the lesions. There is an acute suppurative bronchitis and bronchiolitis, but the epithelium in the bronchi is in large part preserved. The bronchioles and atria are surrounded by pneumonic areas in which the exudate consists almost wholly of well preserved polymorphs. Outside of this the alveoli contain beautiful fibrin nets and the cells are largely desquamated epithelial cells. It is in this zone that reinvestment of the alveoli with new growth of proliferating epithelial cells and occasional organization is encountered. *Large intestine* shows congestion and hypersecretion of mucus. *Testis*: There is an absence of spermatogenesis, and interstitial edema and fibrosis. *Liver, spleen, pancreas, kidney, and myocardium* show no significant lesions.

Bacteriological examination.—*Smears*: *Trachea* shows innumerable small Gram-negative bacilli, a considerable number of Gram-positive diplococci, and a moderate number of fair-sized Gram-negative bacilli. The predominating organism is a small Gram-negative bacillus. *Lung*: Large consolidated portion shows a considerable number of Gram-negative bacilli, a few good sized Gram-negative bacilli. Small consolidation shows very few organisms, small clumps of Gram-positive cocci and a few small Gram-negative bacilli.

NOTE.—Death 14 days after alleged exposure to phosgene. There were no recent mustard-gas burns and the inflammatory changes observed in the trachea and larger bronchi had not the necrotizing character observed in mustard-gas cases. At this stage, it is not possible to make a definite anatomical diagnosis of previous poisoning by asphyxiating gas, although it is quite probable that the extensive bronchopneumonia present may have followed the inhalation of gas. The reparative changes in the bronchi and alveoli were those which might be seen in any type of bronchopneumonia at this stage.

CASE 79.—D. F., 1319851, Corpl., 120 Inf. H. Q. Died, November 2, 1918, at 1.25 p. m., at Base Hospital No. 2. Autopsy, one and one-half hours after death, by Lieut. J. H. Mueller, San. Corps.

Clinical data.—October 20, admitted to No. 61, Casualty Clearing Station. Poisoning by irritant gas, having been exposed October 19 to blue, green, and yellow cross shelling. October 22, admitted to Base Hospital No. 2. Gassed three days ago. Sore eyes and throat. Vomiting. Cough. No burns. Bleeding from nose. Heart normal. *Lungs*: A few coarse bronchial râles. Sputum, mucopurulent. October 25, feels much better. No localization of signs of consolidation; coarse râles and very harsh breath sounds at left base. October 27, fine moist râles over right lower lobe; harsh breath sounds over entire posterior chest. Condition worse, slightly irrational. Sputum culture—pneumococci and micrococcus catarrhalis. October 29, marked dullness with diminished breath sounds over right lower lobe. Fine and coarse râles over left lower lobe. Holding his own. Good pulse. October 31, temperature falling by lysis. Consolidation of both bases. Doing well. November 1, harsh breath sounds with scattered areas of fine râles anteriorly. Respirations 60. Diarrhea. November 2, lemon yellow tint to conjunctivæ and skin. Acute tenderness in right upper quadrant, with rigidity of right abdominal wall. Diarrhea has ceased. No particular change in lungs. Few bronchial râles. Died at 1.25 p. m.

Anatomical diagnosis.—Acute laryngitis; acute purulent bronchitis, confluent double lobular pneumonia; acute fibrinous pleurisy; acute enteritis; hemorrhages into rectus abdominis muscle; icterus. Poisoning with irritant gas.

External appearance.—Slight icterus. No ocular or cutaneous lesions described. Extensive hemorrhages into rectus abdominis muscle.

Gross findings.—*Pleural cavities*: Partially organized adhesions over posterior portions of right and left lower lobe. No fluid. *Left lung*: Covered over entire lower lobe by partially organized layer of fibrin. The bronchi contain much frothy purulent fluid. On section, the greater part of lower lobe presents a very uniform consolidation; the lower portion however, is still free and air containing. The consolidated portion is grayish-red and rather moist. In the upper lobe are a few small areas of bronchopneumonia. *Right lung*: Shows a similar fibrinous exudate over the lower lobe. Bronchi contain rather more

pus than those of the opposite lung, but their mucosa is neither eroded nor hemorrhagic. The lower lobe is completely consolidated, fairly uniform, grayish-red in color; at lower portion, there is a fairly large area made up apparently of small abscesses set closely together; whitish pus may be squeezed from some of these. The upper lobe contains a good many scattered areas of bronchopneumonia, some of them infaret-like in distribution. The middle lobe shows a few areas of hemorrhagic bronchopneumonia. *Organs of neck:* There is very slight ulceration of the glottis, and injection of the vessels near the bifurcation of the trachea; no other changes. *Heart* is normal. *Liver and bile passages* normal. *Spleen* enlarged to about twice normal size, firm, dark purple, follicles prominent. *Adrenals, kidneys, stomach* are normal. *Intestines:* Beginning about half way down the ileum, there is marked congestion of the mucosa without definite ulceration. This continues down to the colon. The solitary lymph follicles are prominent, but not the Peyer's patches. Large intestine normal.

Microscopic examination.—*Trachea and large bronchus:* No section. *Lungs:* The terminal bronchioles are distended with solid masses of purulent exudate in which are bacterial colonies. The epithelium is represented only here and there by proliferating flat cells. There is slight compression of the adjacent alveoli. Between the abscess-like cavities of the dilated atria there is hemorrhagic and fibrinous pneumonia distributed through all portions of the section. The alveoli are being lined actively with new epithelial cells, and here and there are sprouts of fibroblasts and epithelial cells growing into the exudate. There are fair numbers of fibroblasts in the thickened septa also, and occasional large mononuclears. Bacterial stains show large masses of cocci in the purulent exudate which fills the atria. They are chiefly Gram-positive. Elsewhere there are practically no bacteria. Another section of lung shows a uniform, almost lobar type of pneumonic consolidation, without unusual features. *Liver, spleen, kidney:* Marked congestion. *Adrenal:* Loss of chromaffin staining and depletion of cortical lipoids. *Rectus muscle:* Interstitial hemorrhage, without degeneration of fibers. *Small intestine:* Hemorrhages into tips of villi.

NOTE.—Death occurred 14 days after definite history of exposure to irritant gas. When first seen 3 days after gassing, there was slight conjunctivitis, but skin burns were lacking. The patient developed an extensive pneumonia, pathologically in all respects of the influenzal type, and associated with terminal icterus. The upper respiratory passages at autopsy did not show severe and characteristic lesions of mustard gas. There are not sufficient data, therefore, from which to draw conclusions as to the nature of the gas to which the patient had been exposed. It is of interest to note that Case 43, L. K. J., a member of the same organization, gassed on the same day, likewise showed at autopsy lesions which were not typical of mustard gas. It is probable that these patients developed an influenzal pneumonia following a very light exposure to the gas; or else that the lesions followed exposure to a mixture of other irritant and asphyxiating gases. The reparative changes which are a conspicuous feature of the histological picture are also commonly found in the lungs of the primary influenzal cases at this stage.

CASE 80.—M. McM., 1464462, Pvt., Co. B, 129th Field Artillery. Died, October 18, 1918, at 10 a. m., at Base Hospital No. 15. Autopsy, five hours after death, by Maj. Daniel J. Glomset, M. C.

Clinical data.—Mustard-gas inhalation and contact, received in action on October 3, 1918. Second degree burns of legs and right foot. Acute gastritis. Lobular pneumonia.

Anatomical diagnosis.—Lobar pneumonia, red hepatization of entire right lower lobe and parts of the right middle and left lower lobes. Diphtheritic tracheitis and bronchitis. Fibrinous pleurisy.

External appearance.—The face is purplish in color and a large amount of bloody fluid runs from the nostrils. There are deeply pigmented areas over the shoulders posteriorly and the back is black in color. These areas are confluent in places. The sclerae are clear. The pupils are 3 mm. in diameter. There are discrete black patches on the posterior part

of the right shoulder. Body heat is present. Post-mortem lividity is marked. The serotum is unchanged. On the left leg there is a belt of marked pigmentation of the upper and middle thirds and extends down for 4 or 5 cm.

Gross findings.—*Body cavities:* The liver extends 7 cm. below the xiphoid. The diaphragm extends to the 6th rib on the right and to the 5th rib on the left. The pericardial cavity is unchanged. The pleural cavities are unchanged. *Cervical and thoracic organs:* There is a small remnant of thymus left. The lungs are poorly collapsed. The lymph follicles at the base of the tongue are markedly enlarged and almost form two tonsils. The tonsils are large and purplish. There are patches of very adherent membrane in the trachea. These are whitish areas and extend throughout the tracheal wall and also cover the vocal cords. *Left lung* is partly collapsed. The posterior part has a downy feel. Anteriorly there are numerous poorly circumscribed solid areas. In the middle of the lower lobe there is another solid area. The edges of the lobe crepitate. The area in the lower lobe occupies about one-half of the lobe. The surface made by section is purplish-pink in color and rather granular. From the cut surface a bloody tenacious fluid exudes. *Right lung:* The upper lobe crepitates throughout. The middle lobe crepitates posteriorly and the rest is solid. The same large and firm area is in the lower lobe and the lobe contains air at the posterior apex. The surface made by section is mottled and has a purplish-pink color and exudes the same tenacious fluid. *Heart* is normal in size. The myocardium and valves are unchanged. *Abdominal organs:* The spleen is normal in size. The Malpighian corpuscles are fairly distinct. The pulp scrapes off easily. The pancreas is unchanged. The left kidney is soft. The kidneys are markedly swollen and pale. The cortex measures 12 mm. The capsule strips easily. The stomach and small intestines are unchanged. The bladder is unchanged, also the testicles.

Microscopic examination.—*Trachea:* The epithelium is desquamated, save for a few adherent basement cells. There is marked submucous edema without cellular reaction. In the edematous tissue there are great numbers of bacteria. In Gram preparations these are in part Gram-positive coccoid bodies surrounded by a red staining veil or rod-shaped capsule. *Lungs:* In the smaller bronchi, the epithelium is either completely desquamated or the cells are deformed or degenerated. The submucous layer is edematous and infiltrated with polymorphonuclear leucocytes, and other inflammatory cells. The vessels about the bronchi are engorged with blood. Pulmonary capillaries are congested and contain polymorphonuclear leucocytes. The alveoli display pronounced bronchopneumonic process. There are definite groups of alveoli filled with pyenotic polymorphonuclear leucocytes alone and surrounding them are alveoli containing granular debris and red blood cells. Very little fibrin is present. Lymphatic vessels about some of the smaller arteries are filled with pyenotic and fragmented leucocytes. Bacteria are extremely numerous, the predominating type being Gram-positive cocci, sometimes in chains. *Spleen* contains hyaline, pink-staining material in the follicles. No other organs examined.

Bacteriological examination.—*Lung exudate:* Streptococcus hemolyticus, staphylococcus aureus, pneumococcus.

NOTE.—There is a definite history of mustard-gas exposure, 15 days before death, with typical burns. The respiratory lesions, however, were not altogether characteristic of mustard-gas inhalation. There was desquamation of the tracheal epithelium with erosions and massive bacterial infection of the submucous connective tissue. Where, however, the epithelium was preserved it was normally ciliated and showed neither a coagulative necrosis nor the metaplasia commonly found after regeneration. The pulmonary lesions are altogether typical, both grossly and histologically of the pneumonia of the pseudolobar type, which was so prevalent at that time. There was a hemorrhagic, nonfibrinous exudate in which the leucocytes were fragmented and pyenotic; dilatation of the atria with hyaline necrosis of the walls and of the alveolar lining, fibrinous thrombi, and the occasional necrosis of the alveolar capillaries. On the other hand, the customary regeneration and organization which one would expect in mustard gas of this stage were lacking. The lesions

seem too acute for 15 days' duration. It seems probable in summing up the evidence that this patient contracted influenzal pneumonia while in the hospital, and that the initial gas injury of the respiratory tract was negligible except in so far as it may have predisposed to the secondary influenzal infection. It is unfortunate that the clinical history is too incomplete to give further evidence on this point.

CASE 81.—R. J. S., 1426189, Pvt., Co. F, 59th Inf. Died, August 12, 1918, at Base Hospital No. 46. Autopsy No. 3. Autopsy, 11 hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Gassed on July 28, 1918. Burns of forehead and knees. Evidences of gas inhalation complicated with bronchopneumonia caused by staphylococcus albus and nonhemolytic streptococcus. Died with signs of pulmonary edema and symptoms of acute colitis.

Anatomical diagnosis.—Extensive gas burns of conjunctivæ, skin, buttocks, elbows, knees, penis, and serotum. Acute ulcerative and membranous laryngitis, tracheitis and bronchitis. Bronchopneumonia. Moderate pulmonary edema. Acute laryngitis and esophagitis. Acute ulcerative colitis. Slight cardiac dilatation.

External appearance.—Over both buttocks, both knees and the backs of both elbows, the dorsal surface of the penis, the ventral surface of the scrotum, there are characteristic superficial gas burns, extending into the dermis. Those about the knees show near the margin large blebs filled with clear fluid. Elsewhere the base is covered with a thin dry scab. The skin of the backs of the hands and the face has diffuse light brown pigmentation. At the bend of the right elbow there is a small recent surgical incision 2.5 cm. long and gaping somewhat in its midportion. The base covered by an adherent red-brown scab. The superficial glands are somewhat enlarged. The mucous membranes pale. *Eyes:* The eyelids are slightly swollen. The conjunctivæ somewhat edematous and the bulbar portions considerably injected. On the left there are in addition numerous scattered small red hemorrhages. The pupils 5 mm. in diameter. *Ears and nose:* No abnormalities.

Gross findings.—*Pleural cavities:* On opening the thorax, a few thin fibrous bands found binding the apex of the upper lobe to the chest wall on the right side. There is no excess of fluid and no adhesions of the left. The heart lies in normal position. On incising the pericardial sac, no abnormalities of or in the sac noted. *Heart:* Weighs 370 grams. Somewhat enlarged. The right auricle and ventricle slightly dilated. The tricuspid ring admitted three fingers. The valvular endocardium throughout is thin. The coronaries and bases of large vessels, no abnormalities. The left myocardium on section, the architecture regular, the bundles coarser than normal and the tissue pale, boiled. *Right lung:* All lobes voluminous, cushiony and somewhat soggy, especially the upper and lower lobes. The pleura over the lateral and posterior surface, especially of the lower lobe, is somewhat injected and covered by a small amount of tenacious fibrinous exudate. There are a few thin fibrous bands binding the middle lobe to the lower lobe. The glands at the hilum moderately enlarged, pulpy and injected. The vessels at the hilum show no abnormalities. *Bronchi:* There is extensive ulceration of the mucosa and considerable edema and injection of the mucosa. Tightly adherent to the submucosa there is a castlike membrane of friable fibrinopurulent exudate. On section of the upper lobe a moist pink-red surface presents. The air sacs contain a moderate amount of thin frothy fluid. Scattered throughout there are several small solid deep red areas associated with the bronchioles. On repeated section of this lobe the consolidation immediately adjoins not only the small bronchioles but also the good sized ones. The bronchioles throughout show considerable injection of the walls. Attached to the mucosa and submucosa there is an adherent fibrinous and fibrinopurulent exudate. The consolidation about the bronchioles is most marked in the posterior portion of the lobe. The middle lobe, on section, presents a pink surface. The air sacs contain a small amount of thin frothy fluid. The bronchioles show injection of the mucosa. The exudate in this lobe is much less than in the upper lobe. About the bronchioles there is no hemorrhage or consolidation visible anywhere. The lower lobe on section presents a similar picture to that in the upper. There are areas of peribronchial consolidation here, very striking. There is a moderate to considerable amount of fluid in the air sacs. Toward the periphery the lung, especially in the lower portion, shows much more marked areas of peri-

bronchial consolidation, which extends in some places into the lung for a distance of 1 cm. These deep red consolidated areas are more numerous near the pleura in the lower portion of the lobe. *Left lung:* Both lobes are voluminous, cushiony, soggy, especially in the lower. In the lower, scattered solid patches are palpable. The vessels, bronchi, similar to those on the right in appearance. The lymph glands on this side moderately enlarged, pulpy, pigmented, and injected. A number of them show pinhead to small lemon-seed sized firm yellow opaque nodules, encapsulated by firm gray tissue. The left upper lobe similar to the right side, upper, in appearance. The pleura on this side over both lobes especially posteriorly shows a small amount of adherent fibrinous exudate. The lower lobe on section similar to the right lower lobe. The peribronchial consolidation is present to about the same extent. *Liver:* Slight fat infiltration; weighs 2,000 grams. *Organs of neck:* The glands throughout the neck are moderately enlarged, pulpy, and considerably injected. *Thyroid:* Of average size and the tissue, pale, spongy. The acini contain a moderate amount of colloid. *Larynx and trachea:* Show considerable diffuse ulceration of the mucosa, with edema and injection of the submucosa. Overlying intact and ulcerated mucosa there is a considerable amount of friable, tightly adherent fibrinous and fibrinopurulent exudate. The exudate is most marked in the larynx. The folds behind the true vocal cords filled with exudate. The process is present likewise in the upper portion of the esophagus as far down as the pouch at the level of the thyroid cartilage. The mucosa, however, intact, injected and covered by a moderate amount of fibrinous and fibrinopurulent exudate. There is likewise injection of mucosa of the base of the tongue and pharynx with a small amount of exudate. *Tonsils:* Small, buried and scarred. The crypts are clean. *Alimentary tract:* Stomach and small intestines: Show no significant lesions. In the transverse colon there are areas of patchy injection of mucosa, and in places there are small erosions in the mucosa, and in the neighborhood there is an adherent mucopurulent exudate. This mucopurulent exudate peels readily in general. Toward the rectum there are a few small eroded areas above which a friable exudate is quite tightly adherent. The mesenteric glands are somewhat enlarged, pulpy, pale. About the colon, the mesenteric glands show some injection. The remaining organs show no significant lesions.

Microscopic examination.—*Trachea* has a thick partly adherent membrane composed of dense interlacing fibrin strands with pyrenotic nuclear fragments. The surface of the trachea is formed in places by swollen membrana propria which in some areas is reinvested with a single layer of flattened epithelial cells derived from the mucous ducts. Some of these flattened cells appear to be regenerating. In another section, the necrosis of the subepithelial tissue extends about halfway to the cartilage. There are fibrin, hemorrhage, and occasionally small suppurative foci near the surface. In the deeper tissues there are in places proliferating fibroblasts. *Lungs:* Sections show dilatation of the small bronchioles and atria with necrosis of the lining epithelium (see fig. 22), or in some places partial reinvestment with regenerating cells. About these there are extensive hemorrhages with areas of bacterial necrosis. *Medium-sized bronchus* (2-3 cm.): Completely plugged with exudate and membranous. The bronchial wall is entirely necrotic. *Colon:* Section of colon shows no ulceration of inflammatory change. *Kidney, spleen, and liver* show no significant change.

Bacteriological examination.—Smear from the exudate in the trachea shows innumerable organisms, Gram-positive rounded cocci predominating, some in chains, some in diplococcus forms. There are also some Gram-negative cocci and bacilli. Smear from consolidated lung shows a moderate number of Gram-positive cocci in diplococcus formation and small chains. *Cultures* from consolidated lung shows staphylococcus albus, streptococcus non-hemolytic. Culture from *trachea* shows staphylococcus aureus, streptococcus, nonhemolytic.

NOTE.—Mustard-gas case of 15 days' duration. Severe and typical lesions of the upper respiratory tract, with peribronchial hemorrhagic pneumonia. There was practically no reparative change or organization, probably because of the deep seated character of the initial injury. The acute colitis mentioned in the "anatomical diagnosis" is not in evidence in the sections.

CASE 82.—W. J., Corpl., 58th Inf. Died, August 6, 1918, at 6.25 p. m., at Base Hospital No. 18. Autopsy by Lieut. B. S. Kline, M. C.

Anatomical diagnosis.—Shrapnel wound, interseapular region; fracture of spine of two upper dorsal vertebrae, with subsequent infection of wound; septicemia (streptococcus hemolyticus); purulent otitis media, right; anemia and emaciation; general lymphatic hyperplasia; contused wounds of lower extremities and back; remains of old gas burns of penis, scrotum, larynx, trachea, and bronchi; bronchopneumonia (streptococcus and gas bacillus); terminal gas bacillus (?) and streptococcus septicemia.

NOTE.—This case is not reported in detail, inasmuch as the gas burns, incurred at least 15 days before death, were of trivial importance in comparison with the surgical injuries and the ensuing general infection. Although there was no history of exposure to gas, there were characteristic mustard-gas burns noted during life and at autopsy. Histologically, the examination of the respiratory organs was unsatisfactory because of the poor preservation of the tissues and the terminal gas bacillus infection. Nothing was found to indicate previous inhalation of irritant gas. No material from the skin lesions was preserved.

CASE 83.—W. B. P., Pvt., Hdqrs. Co. 6th Marine Corps. Died, June 28, 1918, at 5.30 p. m., at Base Hospital No. 18. Autopsy No. 66, performed 15 hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—None available, and the date of gassing is not recorded. The records of the Chemical Warfare Service show that there were casualties on June 13 in the 78th and 96th Companies of the 6th Marine Corps, which were in action at Belleau Wood and Chateau Thierry. Yellow cross and blue cross gas shells were employed against these detachments.

Anatomical diagnosis.—Bullet wound through right kidney; surgical excision of right kidney; extensive renal hemorrhage (800 c. c.); shock (clinical) and anemia; pulmonary edema (considerable) and slight general anasarca; old gas burns of skin, serotum, and respiratory tract; purulent bronchitis of left lower lobe, associated with moderate atelectasis, following exposure to gas; old tuberculous foci of bronchial and pulmonary lymph nodes.

External appearance.—The skin is pale and slightly sallow. The skin of the neck, upper chest, axillae, upper and inner portions of the thighs, and the bend of the right elbow shows numerous dull light brown splotches, with here and there areas of superficial desquamation. There is slight edema of the ankles. The serotum on its anterior aspect shows a flat smooth surface. The epithelium here appears to be almost entirely gone in a uniform sheet (?); the region is dry. Eyes, nose, and mouth normal. (Description of traumatic and surgical lesions is omitted.)

Gross findings.—*Pleural cavities:* In the right pleural sac there are about 20 c. c. of thin blood-stained fluid; a smaller amount on the left side. No adhesions are present. *Right lung:* Weighs 580 grams. The upper and middle lobes are fairly voluminous, eushiony, slightly soggy. The lower lobe is relatively more voluminous than the others. The pleura is delicate and glistening throughout. There are three small chalky nodules beneath the pleura of the lower lobe on the anterior aspect. The glands at the hilum are considerably enlarged and edematous and show scarred areas. The mucosa of the bronchi is pale; in their lumina is thin frothy fluid and mucus. On section no abnormalities are found except a moderate edema of the upper and middle lobes, and a more marked edema of the lower. *Left lung:* Weighs 630 grams. Both lobes are voluminous; the median portion of the lower lobe feels rubbery. The pleura is thin and delicate. The glands and blood vessels are like those on the right side. The bronchi, however, show a patchy injection of the mucosa, and contain a small amount of viscid purulent material, also thin frothy fluid and mucus. On section, except for edema, the lung is normal with the exception of the mesial third of the lower lobe, where the lung tissue is collapsed, rubbery, dull red, and moist. The bronchial branches in this region contain a considerable amount of viscid mucopurulent material. On squeezing the lung tissue in this region a somewhat translucent viscid fluid exudes. The tissue here is not friable and not more voluminous than the surrounding lung. Examination of the veins and arteries in this region shows no thrombi, the overlying pleura is thin and pale. *Organs of neck, Larynx, and trachea:* Show no abnormalities, except slight diffuse injection in the lower portion of the trachea. In the lumen is a moderate amount of thin

frothy fluid and a small amount of mucus-pus. *Thyroid*, enlarged symmetrically. *Tonsils*: Small and searred. *Heart*: Weighs 335 grams. There is moderate dilatation of all chambers. No other significant changes. *Gastrointestinal tract* shows no significant changes. Remaining viscera show no lesions, except those related to the surgical condition.

Microscopic examination.—*Skin*: There is a thick horny layer. The remainder of the epidermis appears normal and is regularly disposed. There is little or no pigment in the rete mucosum. The papillae are rather loose and show young connective tissue cells and a moderate number of chromatophores filled with golden yellow pigment. The small blood vessels are collapsed and surrounded by loose aggregations of lymphoid cells. The endothelium shows no changes, and there are no thrombi. The deeper layer of the corium and the epidermal appendages are normal. In another block examined, the keratin layer is thin and partly exfoliated. The remaining strata of the epidermis are condensed into a thin densely stained layer in which outlines of individual cells are lost, and the tissue appears mummified or desiccated. There is an apparent increase of pigment in the basal layer. The papillae are flattened out, the corium is very dense and sclerotic, the nuclei pycnotic or caryorrhetic. All superficial vessels are filled with dense hyaline thrombi, having a peculiar refractile appearance. *Trachea and primary bronchus*: The mucosa is largely exfoliated, but detached strips still lying on the surface show excellent preservation of the ciliated cells. The subepithelial connective tissue is edematous in places and moderately congested, but there is no inflammatory infiltration, except for a few round cells. There is therefore no positive evidence of previous gassing. *Lungs*: (a) The lesions are not marked. The septa are stout, and show frequently an accumulation of polymorphonuclear leucocytes in and about the capillaries. Few have emigrated into the alveolar spaces, which contain only desquamated (postmortal?) alveolar cells, either single or in coherent strips, and a little shreddy coagulum. The epithelium of the small bronchi is detached, but shows no degenerative change. There is no exudate in the lumina. There is moderate emphysema. No bacteria are found in Gram-stained sections. (b) Same picture, save that there is partial atelectasis. No evidence of old bronchial lesions. *Liver, myocardium, kidney, and testis* show no significant lesions.

NOTE.—The gas burns, probably inflicted on June 13, 15 days before death, were of minor importance in the case. Death probably resulted from the bullet wound of the kidney, with the accompanying hemorrhage and shock. There is little clear evidence of previous respiratory injury due to the gas, either grossly or in the sections.

CASE 84.—H. G., 2058794, Corpl., Co. G, 47th Inf. Died, October 28, 1918, at Base Hospital No. 42. Autopsy No. 92. Autopsy, 2 hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Patient was gassed on October 12, 1918, having been exposed to blue, green, and yellow cross shells. Admitted to Base Hospital No. 42 on October 25, with burns of skin, conjunctivæ, respiratory tract. Signs of bronchopneumonia in both lower lobes, especially the left. October 27, patient delirious.

Anatomical diagnosis.—Superficial mustard-gas burns of conjunctivæ, scalp, body, scrotum, and penis. Few small vesicles with local brown pigmentation. Acute fibrinopurulent esophagitis extending as far as the cricoid cartilage. Acute fibrinopurulent laryngitis, tracheitis, and bronchitis (left side). Acute purulent bronchitis (right side). Extensive coalescing lobular pneumonia. Acute bronchial lymphadenitis. Cloudy swelling of parenchymatous organs.

Autopsy report.—No detailed protocol.

Microscopic examination.—*Trachea* (2 blocks): The epithelium is not only preserved, but shows remarkably little change. The cells in the superficial layer are cylindrical and here and there distinctly ciliated, although in general they are stained rather poorly. There are a few leucocytes wandering between them. The submucous tissue contains lymphoid and plasma cells in normal numbers, but there is no clear evidence of previous inflammation. Mucous glands are in hypersecretion but otherwise normal. *Primary bronchus*: contains a detached fibrinopurulent membrane about 1 mm. in thickness. The lining is constituted by the exposed membrana propria resting upon edematous and infiltrated granulation tissue. There are a few strips of regenerated, highly atypical epithelial cells interposed between false membrane and membrana propria. The glands are preserved, although they

are separated by edema and inflammatory cells, chiefly of the plasma cell type. *Lungs:* (a) Block, which was apparently taken near the hilus, passes through a group of thick-walled and distinctly dilated bronchi. These are lined for the most part with dense adherent membrane, although, in some places they are reinvested with layers of squamous epithelium. The deeper portion of the bronchial wall, the peribronchial tissue and the original edematous cellular tissue about the blood vessels are the seat of active fibrosis, so that the structures are virtually embedded in a mass of connective tissue. This is rather avascular, the formation of new blood vessels appearing to lag behind the growth of fibroblasts. The adjoining alveoli show the effects of the compression due to the fibrosis of the peribronchial and periarterial tissue. The alveoli contain a serous coagulum with more or less fibrin, showing in places the usual organization. The septa are thickened with new formed fibroblasts and wandering cells, chiefly of the mononuclear type, and are distinctly edematous. The alveolar epithelium projects into the lumina and is probably largely new formed. (b) The smallest bronchioles and atria contain well-preserved epithelium. Some of them show beautiful vascularized organized plugs. A most striking picture is afforded by the organization of fibrin in the interlobular septa, which are already in large part converted into loose vascular scars. The same picture is seen in the loose tissue about the blood vessels. The parenchyma shows a marked diffuse edema of the alveoli with abundant fibrin. This seems to be a recent process. (c) There are several longitudinally cut bronchi completely filled with an exudate, in places purulent, in others purely fibrinous. There is the usual regeneration of epithelium with metaplasia and fibrosis of the wall of the bronchus. The adjoining lung tissue is completely ateleatic. *Skin:* (a) Section passes through an ulcer the base of which is formed by a slough densely infiltrated by masses of leucocytes. The corium is extremely thickened, partly by edema and partly by a new growth of connective tissue and blood vessels. There is not the typical appearance of granulation tissue. The endothelium of the blood vessels is swollen and deeply stained. Mitotic figures are distorted and multinuclear cells are common. There are many small nerve trunks in the section.

The epidermis at the margin of the ulcer is much thickened, especially about the hair follicles. It stops short at the edge of the ulcer and does not seem to be actively proliferating, growing only a short distance between the slough. The epithelial cells at the base are free from pigment. Their arrangement is atypical and they appear to have developed from the sheaths of the hair follicles. (b) Section of skin showing hyperkeratosis and hyperpigmentation with chromatophores in the superficial corium. *Pharynx:* Section shows acute membranous inflammation with separation of the muscle fibres by inflammatory exudate. *Spleen:* Very cellular with excess of polymorphonuclears in the pulp. Appearance is that of the usual acute splenic tumor.

NOTE.—After alleged exposure to yellow, green, and blue cross shells 16 days before death there was found a severe membranous necrosis of the bronchi with partial epithelial regeneration and very extensive early fibrosis of the bronchial walls, periarterial tissue, interlobular septa, etc. The pulmonary lesions were confined to the vicinity except for a diffuse edema, which was probably terminal, or at least of much later date than the bronchial lesions. A peculiar feature of the case was the exemption of the trachea from necrosis, which was so evident in the larger and smaller bronchi. This is difficult to understand and highly exceptional. It is evidently not to be explained by the earlier repair, inasmuch as it is not shown by metaplasia of the usual type which is the rule during the earlier stages of regeneration. There is always the possibility that the blocks may have been confused, but this is unlikely in this case, since tissue examined from different blocks and preserved in different fixative show an identical picture.

CASE 85.—A. A., 1822508, Pvt., Co. C, 321st M. G. Bn. Died, August 27, 1918, at Base Hospital No. 46. Autopsy No. 9. Autopsy, one and three-fourths hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Exposed August 10 at night to heavy shelling with yellow, blue, and green cross gas. On admission to Base Hospital No. 46 on August 11, complained of pain

in chest; respiration was labored; cyanosis and restlessness. Eyelids swollen and edematous. Generalized râles. Patchy fine crackling râles with exaggerated voice sounds at right base. Diagnosis: Gas inhalation, lobar pneumonia. August 14, double lobar pneumonia. Condition fair. August 19, respiration more labored. Signs suggesting fluid at right base, not shown by X ray or aspiration. August 25, no change in symptoms. Signs persist. August 26, pleural friction left base with pains over this region. Signs of patchy bronchopneumonia.

Anatomical diagnosis.—Mustard-gas burns of skin and superficial mucous membranes, healed or healing lesions. Acute ulcerative tracheitis and bronchitis. Fibrinopurulent bronchiolitis. Bronchopneumonia, both lower lobes, in part organized. Extensive fibrinous and fibrinopurulent pleurisy, with effusion and associated atelectasis in both lower lobes. Acute bronchial lymphadenitis. Cardiac dilatation, slight.

External appearance.—*Skin* in general pale, face and hands tanned. Skin of scrotum and base of penis show considerable desquamation; no ulceration, however. There is some desquamation of the skin of the lower abdominal and pubic region and also in the lower right axilla. The superficial mucous membranes, excepting the conjunctivæ, are pale and cyanotic. The superficial lymph glands somewhat enlarged. *Eyes:* Conjunctivæ somewhat edematous, considerably injected. There is a small amount of viscid exudate present between the lids. The pupils, 5 mm. in diameter. *Nose and ears* show no abnormalities.

Gross findings.—*Pleural cavities:* On opening the thorax a small amount of coherent fibrinopurulent exudate found over the right lower lobe. The left chest contains from 1,500 to 2,000 c. c. of turbid yellow fluid, in which flakes of fibrinous exudate are suspended. Both lobes on this side collapsed toward the spine. There is moderate amount of fibrinous exudate binding the median portions of these lobes to the pericardium. On incising the pericardium no abnormalities of the sac are seen. After removing the thoracic viscera the parietal pleura on the left is everywhere glazed, edematous, covered by a considerable amount of shaggy fibrinous exudate. The exudate is most marked over the diaphragm. *Heart:* Weighs 360 grams. Moderate dilatation of both auricles and right ventricle. Myocardium is pale, soft, and moist. *Right lung:* Lobes less voluminous than normal, especially the lower. Upper and middle are cushiony, well aerated. Lower, rubbery. Glands at the hilum considerably enlarged, pulpy, edematous, pigmented. Some show areas of gray scarring. Vessels show no abnormalities. Bronchi somewhat swollen, show areas of injection. In the lumen there is some mucopurulent exudate. On section of the upper and middle lobes a light pink surface presents. Tissues well aerated. In the bronchial branches there is some mucopurulent exudate. In the lower lobe, on section, the tissue is collapsed, rubbery, dull reddish brown, poorly aerated. Scattered throughout the lobe there are large numbers of grape-seed to lemon-seed sized rather firm areas of consolidation. On pressure no exudate is expressed. These areas have a dull grayish-pink surface. Bronchial branches in this lobe contain a small amount of viscid mucopurulent secretion (no organization, apparently). *Left lung:* Both lobes much less voluminous than normal. The pleura is somewhat swollen; covering it, there is a layer of tenacious fibrinous exudate, in places at least 1 mm. in thickness. Between this and the pleura there is a thin zone, which contains many tiny vessels. On section of the upper lobe a well aerated pink surface presents, except posteriorly, where there is an egg-sized dull reddish brown poorly aerated portion. Lower lobe, on section, is similar in appearance to the right lobe. *Organs of neck:* Glands in the lower part of the neck similar in appearance to those at the hilum. *Thyroid:* Of average size and consistence. On section the tissue is pale, spongy. There is moderate amount of colloid in the acini. *Larynx:* Shows a moderate edema of the mucosa. About the left vocal cord there is considerable injection. *Trachea:* Shows patchy injection toward the bifurcation. In the lumen there is some blood tinged mucopurulent exudate. *Tonsils:* Somewhat enlarged, pulpy. Crypts are clean, in general. There is apparently considerable lymphoid tissue present. *Alimentary tract:* No abnormalities except that the lymphoid tissue in the lower ileum is somewhat more prominent than normal. Mesenteric glands pulpy, pale. The remaining organs show no significant lesions.

Microscopic examination.—*Trachea:* No sections preserved. *Lungs:* A. A number of small bronchi included in the section are lined with a very well-preserved layer of ciliated epithelium. Lumina are free from exudate. There is no thickening of the bronchial wall. Parenchyma shows irregular small areas of lobular pneumonia, which appear to center about

the infundibula. Exudate is poor in fibrin. Predominant cell type is polynuclear. About these areas there is some edema and epithelial desquamation. B. This block passes through an infaretlike area of hemorrhage. In certain areas the alveolar structure is destroyed, and there is necrosis with partial decolorization of the red cells. No thrombosed vessels are included in this section. C. Section passes through completely collapsed lung, and includes also large encapsulated areas of caseation with typical giant cells at the periphery. *Liver, spleen, and kidney* show no significant lesions.

Bacteriological examination.—Smears of the exudate in the larynx show innumerable Gram-positive rounded cocci in pairs and in small chains. There are also moderate numbers of Gram-negative cocci. The predominating organism is streptococcus. Culture shows staphylococcus, streptococcus, and small Gram-negative bacillus.

NOTE.—Death occurred 17 days after exposure to mixed gases, but it is not clear either from the clinical history or from the autopsy protocol that this is a late mustard-gas case. There were no typical burns or pigmentation. The eye lesions were no more severe than those frequently seen in influenza. The walls of the trachea and bronchi do not suggest inhalation burns. The patient evidently died from the seropurulent pleurisy complicating the pneumonia. Unfortunately the histological material is inadequate, no tissue from the trachea or large bronchi having been preserved. The excellent preservation of the bronchial epithelium in the small branches is not in common with the usual findings of mustard gas.

CASE 86.—O. F., 1696236, Pvt., Co. D, 305th M. G. Bat. Died, October 13, 1918, 3 p. m., at Base Hospital No. 18. Autopsy No. 135. Autopsy, — hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Mustard-gas inhalation on September 25, 1918, incurred in action. Admitted to Field Hospital No. 306, developed acute bronchopneumonia, of epidemic coalescing type. Mild conjunctivitis, photophobia, and vomiting. September 29, admitted to Base Hospital No. 18, conjunctivitis and serotal burns, few signs of bronchopneumonia. October 10, râles at bases of both lungs, tubular breathing, etc., at left base, bronchopneumonia. October 13, both lungs filled with crackling râles. October 11, blood count, leucocytes 7,800; October 12, leucocytes 8,000. Blood culture sterile; sputum culture, pneumococcus, Type IV.

Anatomical diagnosis.—Healed gas burns of skin. Infected burn of serotum. Acute laryngitis, tracheitis, and bronchitis. Peribronchial pneumonia, in part suppurative, in part organizing. Coalescing lobular pneumonia, right lower lobe. Fibrinous pleurisy, slight. Acute peribronchial lymphadenitis. Cardiac dilatation, right. Parenchymatous degeneration of liver and spleen.

External appearance.—No abnormalities, externally, except moderate diffuse brown pigmentation, with deeper brown pigmentation about the healed superficial ulcerated areas of axillæ and upper portion of left thigh. There are areas of ulceration of the serotum about 4 cm. long, and from a few millimeters to 1 cm. in width extending into the dermis. About these regions the epidermis is thickened for several centimeters and covered by matted serum. There are superficial ulcerated areas about the left nostril, covered by scabs. Conjunctivæ are dry and pale.

Gross findings.—*Pleural cavities:* There is a small amount of fibrinous exudate in the right pleural sac. Left pleural cavity is normal. Pericardium is normal. *Heart:* Weighs 450 grams and is considerably enlarged, the right auricle and ventricle being especially dilated. The myocardium is soft and appears somewhat greasy. *Right lung:* All lobes are voluminous, cushiony, soggy, and solid. The pleura is thin, posteriorly covered by a small amount of fibrinous exudate. The glands at the hilum are greatly enlarged, pulpy, injected. *Bronchus:* The epithelium of the mucosa in general has a whitish appearance. In places there is a patchy ulceration covered by fibrinous exudate. There is considerable diffuse injection with some extravasation of the blood. In the lumen, there is thin and somewhat viscid fluid. In the upper lobe on section, the tissue in general is fairly well aerated. In the posterior half there is a moderate amount of thin, frothy fluid in the air sacs. Throughout the lobe, the striking thing is the involvement of the bronchi, the mucosa having a dull,

ragged, grayish appearance and surrounding the walls there is an area of grayish and red consolidation, a few millimeters in thickness. In places the peribronchial consolidation is depressed grayish, suggesting organization. The middle lobe on section is well aerated and pink. The appearance is quite similar to the upper lobe, but here some of the patches have reached the surface and are bronchopneumonic in type, finely granular, and yellowish gray. On section of the lower lobe the picture is that of extensive involvement of the bronchial mucosa and walls and adjoining lung tissue. There are depressed, firm, grayish streaks. Toward the pleura posteriorly there is a finely granular, gray-red consolidation, coalescing lobular in type. The process, however, is not very extensive. The fibrinous exudate over the pleura is perhaps most marked in this region. The smaller bronchioles in many places contain thin viscid purulent exudate. *Left lung:* Both lobes are voluminous, cushiony, and soggy solid. The posterior portion is most involved. The bronchi and glands similar to those on the right. On section of the upper lobe, the smaller bronchioles show a dull whitish, in places granular, membrane. In the lumen there is thin viscid pus. In places, there is considerable destruction of the bronchial walls with dilatation. There is old peribronchial consolidation, coarsely granular in some places, softened in others. The consolidation is practically limited to the posterior half. Medially, the tissue is well-aerated pink. The lower lobe, on section, shows quite uniform involvement of the smaller bronchial branches and the lung tissue about them for a small distance. There is a moderate amount of thin, frothy fluid in the air sacs. *Organs of neck:* The larynx shows considerable injection of the mucosa. The epithelium in considerable part is dull, whitish, apparently necrotic. There is mucopurulent exudate present in considerable amount, especially about the true vocal cords, where the ulceration seems to extend deeper into the mucosa in places. Throughout the trachea the membrane in considerable part has a dull grayish appearance. There are areas of desquamation. There is patchy injection, and in places, the mucosa shows purulent ulceration. The process involves the base of the tongue, posterior pharynx, and upper esophagus as far as the level of the cricoid cartilage. *Thyroid:* Moderately enlarged, the acini distended with colloid. *Liver:* Weighs 2,000 grams. There is slight fatty infiltration. *Spleen:* Weighs 400 grams, somewhat enlarged. Malpighian bodies increased in number and size. *Alimentary tract:* Not recorded. The remaining organs show nothing of interest.

Microscopic examination.—*Trachea:* Section is not instructive. Submucous layer is thin and intact and stains poorly but does not seem to be necrotic. The membrana propria is preserved. A few faintly-staining vertically arranged epithelial cells are still adherent but the greater part of the epithelium has been desquamated. *Large bronchus:* The surface epithelium is largely lost. A few small strips of stratified, nonciliated epithelium are still adherent, but in most places the membrana propria lies exposed. The striking feature is the presence of solid masses of epithelial cells, of concentric arrangement and highly atypical character. These are situated in the ducts and acini of the mucous glands. (See fig. 19.) In some places the intercellular fibrils complete the resemblance to epidermal cells. This atypical epidermis elsewhere surrounds or penetrates masses of mucus and the remains of the original gland cells. There is marked congestion of the epithelial tissue, but no polynuclear infiltration. *Lungs:* Section includes a medium-sized bronchus, the wall of which is lined with necrotic tissue, adherent to which are shreds of atypical layered epithelium. The bronchial wall is formed by granulation tissue, very loose, vascular and hyperemic with fibroblasts and plasma cells. About the bronchus, the alveoli contain plugs of dense poorly-staining fibrin which in a few areas show early organization. The alveolar epithelium, is swollen, atypical and hyperplastic. Mitotic figures are found in a few of the cells. Plasma cells are numerous. Other areas in the section show nonfibrinous homogeneous conglutination and in still other areas there is an acute pneumonic exudate. The interlobular septa are edematous. *Skin:* Probably of serotum. There is a slight hyperkeratosis, hyperpigmentation of the rete mucosum and numerous melanophores in the superficial layers of the corium. (See Pl. V.) *Myocardium, liver, and kidney* show no significant lesions.

NOTE.—Mustard-gas poisoning of 18 days' duration. There are the usual remains of an acute destruction of the upper air passages, with extensive complicating pneumonia showing early regeneration in the vicinity of the bronchi. The most interesting histological features are the nests of carcinoma-like epithelial cells in the bronchial ducts and glands.

CASE 87.—W. S., 1821307, Corpl., 318th Inf. Died, October 24, at 8.12 p. m., at Base Hospital No. 81. Autopsy, 15 hours after death, by Capt. B. S. Kline, M. C.

Clinical data.—October 5, 1918, patient admitted to Gas Hospital No. 1. October 7, admitted to Base Hospital No. 81. Diagnosis: Gas inhalation, marked. While in the hospital, developed signs of influenza (October 15) and of bronchopneumonia (October 17). Acute temporary dilatation of heart. Leucocytes (October 10) 5,700. Leucocytes (October 15) 6,600. Patient apparently convalescing. October 24, at 8.12 p. m., suddenly began gasping for breath and died a few minutes after.

Anatomical diagnosis.—Healing acute tracheitis and bronchitis; stenosis of right bronchus due to scarring (old infected mustard-gas lesion); healing acute lymphadenitis of mediastinal and tracheal lymph glands; fat infiltration of myocardium; cardiac dilatation, most marked on right side, with possible slight hypertrophy of right ventricle; chronic passive congestion of short duration, of abdominal viscera; thrombosis of left iliac vein; large emboli occluding pulmonary artery; old tuberculous foci of bronchial lymph glands and spleen.

Microscopic examination.—*Pharynx or upper esophagus:* Stratified squamous epithelium, showing nothing atypical. Subepithelial tissue free from inflammatory changes. No lesions suggesting previous injury. *Primary bronchus:* Lined with regenerated squamous epithelium, the superficial cells of which are flattened and deeply stained, with indistinct nuclei, appearing almost as if keratinized. Mitoses are very numerous at all levels. The subepithelial tissue is loose and vascular, loosely infiltrated with mononuclear lymphoid and plasma cells. The mucous glands are not much altered; some acini seem to be choked with retained mucus. *Lungs:* Many of the bronchioles contain still a purulent exudate. Their lumina are narrow in proportion to the thickness of the wall, which is formed by granulation tissue, thickly infiltrated by lymphoid and plasma cells. The surrounding alveoli are thick-walled, often collapsed, and frequently lined with high columnar or atypical epithelium and filled with plugs of organizing exudate. Outside is a zone of edematous lung tissue and between these areas of peribronchiolitis, there are areas of emphysema. The periarterial tissue is tremendously thickened with young fibroblasts in abundance, and the interlobular septa are also. There are in some of the sections, large patches of granulation tissue in which the original lung structure is completely lost. The epithelium in bronchioles and alveolar ducts is wholly missing in some cases, in others there is regenerating epithelium, more or less atypical in character. No bronchi lined with well-ciliated epithelium are found. *Bronchial lymph nodes:* Contains a large calcified encapsulated mass, probably a healed tuberculous lesion. The lymph sinuses in the intact portion of the gland are filled with phagocytic cells. *Spleen:* Congested; no features of special interest.

NOTE.—The interpretation of this case is difficult. The healing lesions of the bronchi, found at autopsy and confirmed by microscopic examination, were ascribed by the pathologist to the late effects of mustard-gas inhalation. However, there is no record in the history of mustard-gas burns or eye lesions, and none are included in the very detailed anatomical diagnosis. On the other hand, there is a clinical history of influenzal pneumonia, the onset of which dates from October 15, approximately 10 days after the alleged exposure to gas, and nine days before death. The patient was convalescing from this, but died suddenly from pulmonary embolism, following thrombosis of the iliac vein, a not uncommon influenzal complication. The question arises, therefore, whether the bronchial and pulmonary lesions were late sequels of the influenzal pneumonia, or were attributable rather to the previous gassing. While it is hardly possible to be certain, it seems more probable that the gassing was responsible, at least in large measure, since the thickening of the bronchi and the extensive fibrosis in some areas of the lung tissue itself were beyond what might ordinarily be expected to develop within nine days of an influenzal pneumonia.

CASE 88.—W. C. D., 2178762, Corpl., Co. B, 354th Inf. Died, August 28, 1918, at Base Hospital No. 42. Autopsy No. 2. Autopsy, eight hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Exposed to yellow, blue, and green cross shell from 10.30 p. m., August 7, to 3.30 a. m., August 8. Ten thousand 77 and 105 mm. shells. August 9, admitted to Field Hospital No. 327, with temperature of 104°. August 11, admitted to Base Hospital No. 42. August 13, temperature 104°. Diffuse râles in both lower lobes. Impairment of resonance in lower loft. No tubular breathing. On following day, râles over upper lobes also. Two days later, bronchovesicular breathing in both. This persisted for five days. August 26, signs of consolidation in right, middle, and lower lobes. Death with signs of cardiac dilatation.

Anatomical diagnosis.—First-degree mustard-gas burns of skin. Healing lesions with areas of vesiculation and brown pigmentation. Ulceration of upper esophagus, larynx, trachea, and bronchi. Fibrinopurulent esophagitis, laryngitis, tracheitis, and bronchitis. Bronchopneumonia in part organized. Acute fibrinous pleurisy. Acute bronchial lymphadenitis. Slight pulmonary edema. Cardiac dilatation.

External appearance.—*Skin* in general has a muddy appearance. The ventral surface of the scrotum and the head of the penis show an ulceration of the epidermis. There is considerable desquamation. A small area of the scrotum shows some matted seropurulent exudate. There is considerable exudate covering the ulcerations of the head of the penis. Over the right greater trochanter there are some pustules and small areas of superficial ulcerations covered by brown scabs. In the genital folds, the popliteal regions, both buttocks, the bends of the elbows, both axillæ, upper chest and neck, there is well defined, splotchy, brown pigmentation. Associated with all of these areas there are tiny vesicles. The superficial lymph glands are somewhat enlarged. Superficial mucous membranes are pale. *Eyes:* Conjunctivæ in general pale, delicate. There is some swelling of the bulbar conjunctivæ, and there is a small amount of eaked exudate present. Pupils equal 3 mm. *Ears:* In the skin of the right ear, near the concha, there is a small superficial ulcerated area about 2 mm. in diameter, covered by a dry scab. There is also a small ulcerated area at the junction of the upper and lower lips. In the nasal cavity there is some mucopurulent exudate.

Gross findings.—*Pleural cavities:* On opening the thorax, a few organizing adhesions are found over the upper lobe. In the cavity there are about 40 c. c. of turbid yellow fluid in which some flecks of exudate are visible. A similar picture is present on the left, except that there are no firm adhesions. Heart lies in normal position. On incising the pericardium no abnormalities of or in the sac are seen. *Heart:* Weighs 380 grams. There is slight dilatation of both right and left ventricles. *Right lung:* All lobes are much more voluminous than normal. Feel cushiony, slightly soggy, and numerous small solid patches are palpable. Pleura, except medially, glazed, covered by a small amount of fibrinous exudate. Glands at the hilum are greatly enlarged, pulpy, injected, pigmented. A number of them show firm and calcified nodules, surrounded by firm gray tissue. Vessels at the hilum, no abnormalities. *Bronchus:* Shows considerable swelling, injection, and in places ulceration of the mucosa. The membrane is infiltrated and covered by tenacious fibrinopurulent exudate in considerable amount. The upper lobe on section shows innumerable solid patches, varying in size from pinhead to a few centimeters in diameter. Some of the smaller areas are coherent, dry, granular, grayish, or yellowish; some have soft yellow centers. Others are much more firm, gray, and show a greenish pigmentation about them. The larger patches are dull pinkish gray. The surface is relatively dry, finely granular. The remainder of the lung tissue is fairly well aerated, pink, and contains a small amount of fluid in the air sacs. Middle lobe, picture in general similar, especially posteriorly. Medially, there is much less involvement. Lower lobe, the picture is quite uniform throughout. Tissue in general fairly well aerated, pinkish red, contains a small amount of thin frothy fluid in the air sacs. Here, quite thickly throughout, there are pinhead to grape-seed sized firm patches of consolidation, some gray, others showing considerable greenish pink pigmentation. In a few places, especially inferiorly, there are larger dull pinkish-gray consolidated areas. Some of the bronchial branches show intense injection of the mucosa and walls. *Left lung:* Both lobes are much more voluminous than normal. On inspection, palpation, and section the upper lobe shows changes similar to the right upper; here, however, there are but few large patches of recent consolidation. In great part the lesion consists in a moderate number of firm solid patches. Left lower lobe, in general similar to the right lower. There is more fluid in the air sacs on the left. The glands at the hilum similar in appearance to those on the right. The tuberculous foci here, however, less prominent. The bronchi show very much less involvement than the bronchi and larger branches on the right.

Organs of neck: Glands in the lower portion of the neck, similar in appearance to those about the hilum on the right. Some show old tuberculous foci. *Thyroid:* Somewhat smaller than normal. Tissues, spongy and pale. There is but a moderate amount of colloid in the acini. *Larynx:* Shows small ulcerated areas of the epiglottis, ulceration extending down into the submucosa. Vocal cords show ulceration of the epithelium. The epithelium in general is infiltrated or ulcerated. Everywhere below the true cords there is a large amount of tenacious fibrinopurulent exudate. Picture the same in the trachea. The process continues over into the upper esophagus, where there is a large patch of ulceration of the epithelium, and a considerable amount of tenacious fibrinopurulent exudate attached to submucosa

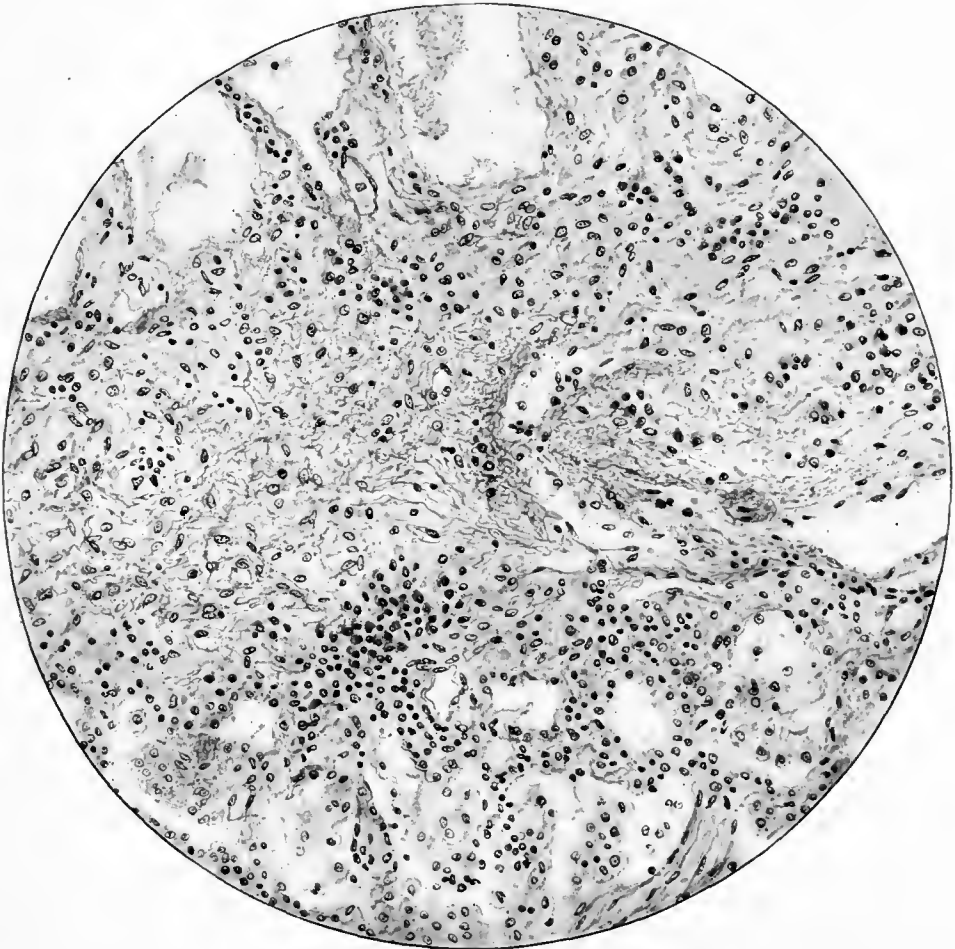


FIG. 34.—Case 88. Exposure to yellow, blue, and green cross shell gas. Death after 20 days. Lung. Section passes through interlobular septum, which is edematous and in which there is active growth of fibroblasts, and plasma cell infiltration. There are organizing plugs in the septal lymphatics

tissue. *Tonsils:* Fair size, contain a considerable amount of lymphoid tissue. Crypts contain inspissated material. *Alimentary tract:* No abnormalities, except that the stomach contains a small amount of bile-tinged mucus. Lymphoid tissue throughout the trachea slightly more prominent than normal. Mesenteric glands are small, pulpy, and pale. *Liver:* Weighs 2,000 grams. Slight fat infiltration. The remaining organs show no significant lesions.

Microscopic examination.—*Trachea:* No sections. *Bronchi:* Section through a medium-sized bronchus shows massive necrosis of the lining without definite membrane formation. Through the necrotic tissue there is a great amount of detritus. The epithelial layer is

totally destroyed, although the mucous glands are still intact. In the deeper part of the bronchial wall, there is active proliferation of fibroblasts and great numbers of plasma cells. There is much fibrinous edema in the peribronchial tissue external to the cartilage, and in these areas are many fibroblasts. One of the small veins contains a well formed thrombus which is beginning to organize. *Lung*: The lesions in the smaller bronchi are very interesting. Some of the bronchi are lined with a clean vascular granulation tissue, uncovered by epithelium. There is no exudate in the lumen. Between the congested vessels are numerous lymphoid and plasma cells, but practically no polynuclears. About these bronchi, the septal tissue of the alveoli is thickened. Many of the air spaces are filled with dense fibrin plugs which are being invaded by fibroblasts and recovered in many places by alveolar cells, probably regenerated epithelium. (Fig. 34). Other bronchi are clothed with regenerated epithelial lining, continuous with solid plugs of epithelial cells in a neighboring alveoli. New formed epithelium is highly atypical, stratified, and nonciliated. The lumen contains well-preserved polymorphonuclears. There is a new formed epithelial lining resting upon a layer of clean granulation tissue, in which are only occasional Gram-positive cocci. Still other bronchi show early and very acute lesions. Lumen is filled with fragmented polymorphonuclears and the walls are invaded by them. There are small areas of bronchopneumonia in the adjoining alveoli. The grayish-yellow nodular areas described in the gross resolve themselves into bronchioles or infundibula, the center of which is occupied by exudate with numerous fragmented leucocytes. The wall is greatly thickened, partly by inflammatory infiltration, but also by an active growth of granulation tissue with strikingly numerous plasma cells. The adjoining alveoli are solid with fibrin plugs becoming organized and covered with new alveolar epithelium. External to these peribronchial nodules, the lung tissue shows a patchy edema. In some areas, the alveolar septa are greatly thickened by the growth of fibroblasts along the collapsed capillaries, and the accumulation of mononuclear cells. The cavities are being relined with new epithelium. The interlobular septa are broad and there are numerous fibroblasts invading the edematous tissue. An interesting feature is the organization of plugs of exudate in the dilated septal lymphatics. (Fig. 34.) The remaining organs show no significant lesions.

Bacteriological examination.—Smears of the trachea show innumerable Gram-positive cocci, some lancet-shaped, others rounded and in chains. The lancet-shaped ones encapsulated. There are also a moderate number of Gram-negative bacilli. The predominating organism, Gram-positive. Smear of consolidated lung shows a very few diplococci (Gram-positive) and no Gram-negative organisms are seen.

NOTE.—A very characteristic case of mustard-gas poisoning dying after 20 days. The respiratory lesions were largely limited to the trachea and the bronchial and peribronchial tract. Although many of the bronchi still showed evidence of the original chemical injury in the form of a deep-seated necrosis, attempts at repair were well under way. In some of the tubes, there was partial reepithelization and the walls of the bronchi as well as the perivascular tissue and the edematous interlobular septa were becoming thickened by a new growth of fibrous tissue. The case illustrates clearly the probable nature of the permanent injury which may follow this type of gassing. It is worth recording also that the lesions do not suggest a complicating influenzal pneumonia, such as was so frequently encountered in the October and November cases.

CASE 89.—W. K., 1779786, Wagoner, 308th Inf. Died, October 28, 1918, at 2 a. m., at Base Hospital No. 42. Autopsy No. 91. Autopsy, seven hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Gassed on October 8, 1918. Admitted to infirmary on October 10. Diagnosis: "Mustard-gas inhalation." On admission to Base Hospital No. 42 on October 18 complained of cough and fever. Symptoms of laryngitis, bronchitis, and bronchopneumonia; signs of consolidation of both lungs.

Anatomical diagnosis.—Superficial gas burns of conjunctivæ and skin with vesiculation and local brown pigmentation. Infected scrotal burns. Acute fibrinous and gangrenous laryngitis with marked ulceration of vocal cords. Gangrenous tracheitis and bronchitis.

Extensive peribronchial pneumonia of all lobes except right middle, associated with ulceration of bronchi and adjoining lung tissue. Gangrenous exudate in cavities. Acute bronchial lymphadenitis. Parenchymatous degeneration of liver and kidneys. Moderate anemia and emaciation. Dental caries marked.

No detailed autopsy protocol received.

Microscopic examination.—*Skin*: Section passes through an area in which the epithelium is denuded; the exposed corium appears dense as if dessicated. Adjacent to it, the epithelium is greatly thinned out; there is a homogeneous pink-staining material beneath the thin layer of epithelium, which is apparently regenerating. There are still in places, adherent crusts of



FIG. 35.—Case 89. Mustard-gas burn, 20 days' duration. Lung. Area of bacterial necrosis with fibrinopurulent material in the adjacent alveoli

completely necrotic tissue. There is marked hyperemia of all the vessels, little leucocytic reaction. (See fig. 5.) *Trachea*: Is denuded of epithelium over large areas, where the lining consists of necrotic tissue chiefly infiltrated with leucocytes, the nuclei of which are much fragmented. There are adherent shreds of fibrinous slough and masses of bacteria. Where the epithelium is preserved, it consists usually of a single row of cuboidal cells resting upon a swollen hyaline membrane. In a few places the cells are heaped up into several layers, suggesting proliferation (mitoses). An interesting feature is noted in one section where the regenerating epithelium has interpolated itself beneath the still preserved, swollen, original membrana propria and a new basement membrane seems to be in process of formation. (See fig. 18.) There is an active growth of cells from the mucous ducts, forming solid

sheets of large polygonal, nonciliated cells. The mucous glands are in hypersecretion. In one duct, the cavity or widened lumen is filled with a mass of desquamated mucous cells.

Lungs: The infundibula and terminal bronchi show gangrene of their walls including often the neighboring alveoli. The nuclei have lost their staining, and there are large masses of bacteria. (Fig. 35.) There is much brownish-black pigment, both extra and intracellular. Elsewhere there is a loose pneumonic exudate, more or less hemorrhagic or fibrinous. Some alveoli are filled with fragmented vacuolated cytoplasm. (Fig. 36.) There is little or no regeneration or organization evident. A very interesting appearance is afforded by the lifting up of the alveolar epithelium in continuous sheets, with accumulations of leucocytes underneath. *Adrenals:* There is marked congestion with capillary extravasation. *Spleen:* Presents the usual picture of an acute splenic tumor.

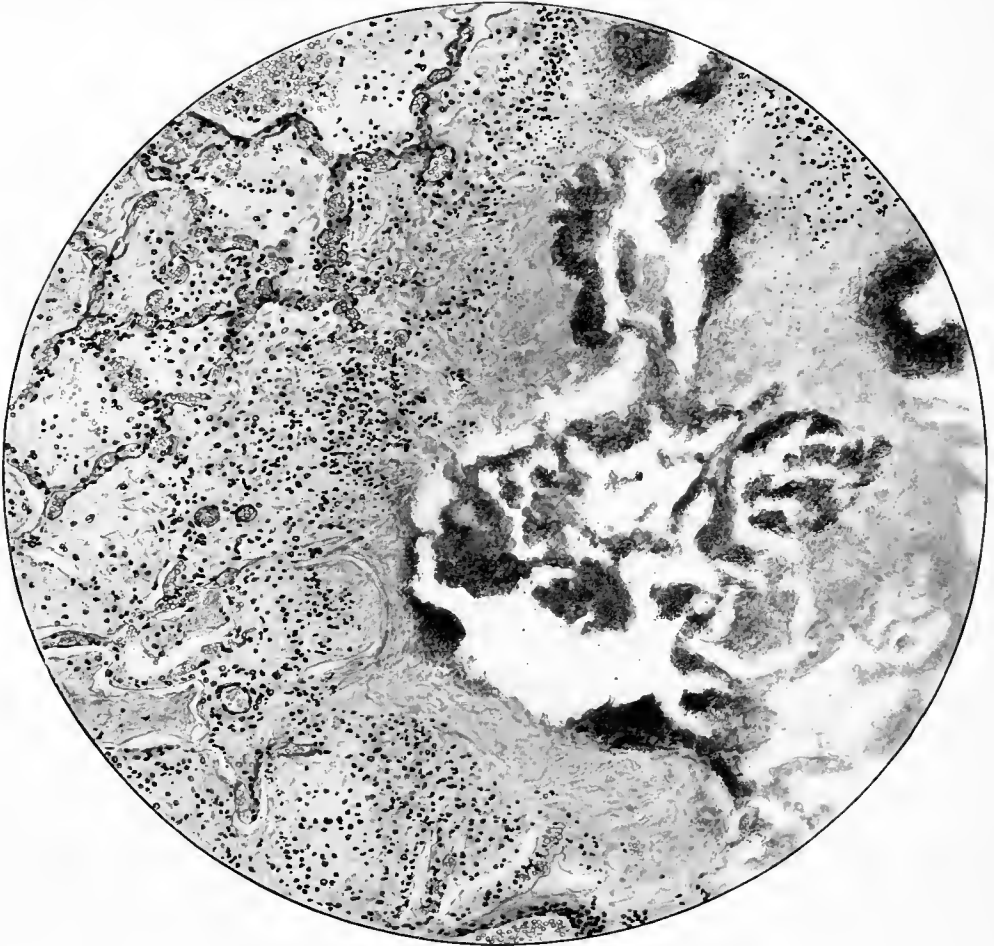


FIG. 36.—Same as Fig. 35. Larger area of gangrene in lung

NOTE.—Case of mustard-gas poisoning of 20 days' duration. Although certain of the bronchi showed regeneration of the epithelium with metaplasia, the majority of them, as well as the trachea itself, were the seat of a gangrenous necrosis, associated with the presence of great masses of bacteria. There was a gangrenous infection of many of the infundibula extending into the adjacent lung tissue. About these necrotic areas there was a fibrinous pneumonia with organization. The presence of marked dental caries is specifically recorded and may have some relation to the gangrene.

The following points of special histological interest may be noted: In the skin, the regeneration of the nonpigmented, atypical epithelium beneath the vesiculated crust of the original epithelium, absence of hair follicles, and marked vascular dilatation. The regeneration, in the bronchus, of the epithelium beneath the still preserved hyaline basement membrane. The gangrenous bronchitis and bronchiolitis in the lung.

CASE 90.—L. M., 1202584, Pvt., 102d Engineers. Died, November 4, 1918, at 12.55 a. m., at Base Hospital No. 2. Autopsy, 10 hours after death, by Lieut. J. H. Mueller, San. Corps.

Clinical data.—October 29, admitted to General Hospital No. 1. Gassed on October 8; in hospital for mustard-gas burns. While in hospital, suddenly developed chills, fever, pains, sore throat, and cough. On admission, general condition excellent. Slight conjunctivitis. Heart normal. *Lungs:* No dullness, breath sounds normal. Tenderness in patellæ, shins, and back. October 30, seem to be worse. Temperature up last night. Lungs show areas of dullness, more on right side posteriorly; many moist râles over both lungs. November 2, has been growing progressively worse, with more and more involvement of lungs. Heart action rapid, cyanosis marked. November 3, has become more cyanotic, with grayish pallor; respirations weak, shallow, and rapid. Heart action poor; edematous breathing. November 4, died at 12.55 a. m.

Anatomical diagnosis.—Acute tracheobronchitis; confluent lobular pneumonia; edema of lungs; hemorrhages into pleura.

External appearance.—No cutaneous lesions.

Gross findings.—*Pleural activities:* No fluid. *Left lung:* Pleura smooth; there are punctate hemorrhages over the lateral surfaces of the upper and lower lobes. *Bronchi:* Contain abundant thin frothy fluid. The larger vessels are normal. On section, the lung tissue is very wet; there is a confluent lobular consolidation throughout the greater part of the lower lobe and the base of the upper lobe; the consolidated portion is red, with mottled lighter areas. The smaller bronchioles do not contain pus. *Right lung:* Covered with smooth pleura. Bronchi also contain frothy fluid; their mucosa is intensely injected. On section, the same type of consolidation described in the opposite lung is found throughout the lower lobe, the base of the upper, and about half of the middle lobe. *Organs of neck:* *Larynx* normal. *Trachea:* Shows a rapidly increasing injection of the mucosa without ulceration, as it descends. *Heart* normal. Remaining viscera show no significant lesions. *Stomach and intestines* normal.

Microscopic examination.—*Trachea and primary bronchus:* No sections. *Lungs:* The small bronchi show partial exfoliation of the epithelium in long strips. The individual cells are not necrotic. The lumina contain polymorphonuclear leucocytes, red blood cells, and granular coagulum. The bronchial walls are infiltrated with leucocytes. The parenchyma shows a most intense congestion of the alveolar capillaries, with widespread hemorrhagic edema. The alveolar spaces contain a varying number of rather pycnotic and fragmented polymorphonuclears, and occasional pigmented alveolar cells. Some areas show only hemorrhage and edema. There is much destruction and caryorrhexis of the capillary endothelial nuclei, the nuclear material being drawn into long wisps and threads. The infundibula are dilated, and the walls show, not infrequently, hyaline necrosis. The pleura is normal. The interlobular and periarterial lymphatics are distended; some contain masses of inflammatory cells. Sections stained for bacteria show minute Gram-negative bacilli within the leucocytes, in considerable numbers. No other bacteria found in careful search. *Liver, spleen, and kidneys:* No significant lesions other than congestion. *Adrenal:* Impoverishment of lipoids in cortex, with degeneration of individual cells. Poor chromaffin staining.

NOTE.—The case is of interest, since it illustrates the occurrence of an influenzal pneumonia in a gassed patient, 21 days after the gassing. A study of the gross and histological lesions indicates that the influenzal pneumonia is probably a primary infection, not related to the gassing. The bronchi fail to show the usual epithelial necrosis, followed by metaplasia, and there are not

the customary peribronchial lesions of mustard gas. The lesions, on the other hand, are in all respects typical of the influenzal pneumonia which was raging at that time.

Another point of interest in the case is the presence, apparently in pure culture, so far as can be judged by the section, of a minute Gram-negative influenza-like bacillus.

CASE 91.—J. W., 1910957, Sergt., 328th Inf. Died, October 26, at 8.25 p. m., at Base Hospital No. 46. Autopsy, 13 hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—October 3, admitted to Field Hospital No. 325; diagnosis; acute bronchitis. Admitted to Base Hospital No. 46 on October 5. Onset of illness October 1, with cough and aching of body. Breathing shallow, rapid, and labored; cyanotic. Lungs negative except in left axilla, where there is bronchial breathing, and showers of râles in left upper lobe posteriorly. The right and left lower lobes are consolidated. October 14, very nervous, cyanotic, delirious, pulse weak and thready. Died, October 26. Leucocytes on October 7, 3,900.

Anatomical diagnosis.—Vesiculation of skin in folds of flanks (old gas burns ?); healed ulcers of vocal cords; acute tracheobronchitis; extensive peribronchial pneumonia, all lobes showing areas of resolution and organization; bronchiectasis; left lower lobe; coalescing lobular pneumonia, left upper lobe; fibrinous pleurisy with effusion (400 c. c.); pulmonary edema, moderate; cardiac dilatation, right; abscess of right arm, following hypodermic injection. A detailed autopsy protocol of this case was not made, owing to stress of other work (personal communication from Lieutenant Kline).

Microscopic examination.—*Trachea:* Epithelium desquamated, either superficially or completely, exposing the membrana propria. Where the superficial cells are still present they are normally ciliated and appear uninjured. It is probable that the loss of epithelium is a postmortal affair. The subepithelial tissue is normal save for congestion. *Lungs:* (a) The picture is complicated. Some of the bronchioles are dilated, but lined with well-preserved ciliated epithelium. The walls are thickened, congested, and densely infiltrated with lymphoid and plasma cells, but there is no exudate in the lumen. Other bronchioles show acute inflammatory changes. The epithelium is more or less completely detached, the lumen filled with pus and exfoliated cells; there is intense congestion and in some cases free hemorrhage beneath the epithelium, and a dense infiltration of the wall with polymorphonuclears. About these infected bronchi are patches of pneumonia, at the periphery, of which, organization of the exudate, which is here more purely fibrinous, is in progress. Between the pneumonic patches, there is intense congestion, with partial collapse. There are many pigmented cells in the alveoli, and a general stasis of leucocytes in the capillaries. (b) Pleura shows a fibrinous exudate, with beginning ingrowth of fibroblasts at the base. The subpleural lymphatics are filled with purulent exudate. There are no larger bronchi in the section, but the bronchioli and the ductus alveolares are dilated with pus, and show necrosis and partial degeneration of their epithelium. The parenchyma shows diffuse fibrous and edematous thickening of the alveolar septa, with round cells and polymorphonuclears between the epithelium and capillary walls; extensive relining of the alveoli with columnar, probably regenerated epithelium; plugs of freshly organizing exudate in the alveolar spaces, or more recent fibrinous exudate with numerous exfoliated alveolar cells. (c) Some of the small bronchi show complete necrosis of their wall, and their somewhat narrowed lumina are filled with pus. The adjoining lung tissue is atelectatic, and shows extensive septal fibrosis and organization. The predominating types of wandering cells are the lymphoid and plasma cells. There is marked periarterial fibrosis. The section includes several bronchiectases, lined with ciliated epithelium. The prevailing bacteria in Gram-stained sections are Gram-positive cocci in pairs and chains. *Bronchial lymph nodes:* Contain masses of resorbing exudate in the sinuses.

NOTE.—Presumably a late case of mustard-gas poisoning, dying 23 days after exposure. The skin lesions were suggestive of old mustard-gas burns. The trachea gave no positive indication of gas injury, but the lung showed lesions of the bronchioles (necrosis, thickening, stenosis, bronchiectasis) which pointed strongly to previous gas injury. The marked leucopenia (3,900) on the fourth

or fifth day after the supposed gassing was confirmatory evidence. The lesions were not quite those following in the wake of influenzal pneumonia, although the case occurred during the period when the epidemic was at its height, and a primary influenzal infection can not be entirely ruled out. The case illustrates the difficulty in arriving at a positive conclusion, when definite data as to the gas exposure are lacking.

CASE 92.—H. R., 489127, Pvt., 34th Inf. Died, November 7, 1918, at 10.30 p. m., at Base Hospital No. 81. Autopsy, 11½ hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—Exposed on October 14 to yellow and blue cross shells. October 17, admitted to Base Hospital No. 78 with diagnosis of bronchitis. Diagnosis had been made at Infirmary No. ? of influenza and gas burns about eyes. October 23, admitted to Base Hospital No. 81. Complaints of pains across chest and cough; has been somewhat deaf for about two weeks. There is some impairment of resonance over right chest posteriorly below the angle of the scapula; also in right lower axilla. Over right base and lower axilla, there are many fine moist râles; scattered dry râles throughout the chest. October 23, leucocytes 15,600; November 2, leucocytes 15,400; November 6, leucocytes 13,600. *Clinical diagnosis:* Bronchopneumonia.

Anatomical diagnosis.—Gas burns of respiratory tract; healing ulcerative tracheitis and bronchitis; acute and organizing bronchopneumonia, all lobes; fibrinopurulent pleurisy, right; cardiac dilatation, right; terminal pulmonary edema, moderate; acute splenic tumor.

No detailed autopsy protocol was made in this case, owing to stress of other work (personal communication from Lieutenant Kline).

Microscopic examination.—*Primary bronchus:* There are adherent strips of stratified, but ciliated epithelium, showing no necrosis. There is an acute inflammation with leucocytic infiltration and congestion and edema of subepithelial tissue. The wandering cells are chiefly lymphocytes. *Lungs:* The larger bronchi are completely lined with ciliated epithelium, which, however, is composed of several layers like that of the trachea. There is mucopurulent exudate in the lumina. The wall is replaced by granulation tissue, densely infiltrated with lymphocytes. Most interesting changes are found in the smallest bronchioles and atria. Many of them are obliterated in part by purulent exudate, in part by ingrowing vascularized plugs of organized tissue. Their walls are thickened by granulation tissue. The surrounding alveoli are collapsed and show the usual epithelial changes and organization of contained exudate. Between these foci of bronchitis and peribronchitis, the lung tissue is emphysematous, and the air spaces free from exudate. In another block, the pleura is included. It is covered with a thick layer of fibrinous exudate, which shows only beginning organization. The underlying lung tissue, including also the bronchioli, is collapsed. The bronchi are lined with well-preserved ciliated epithelium; they contain mucopus, and in places there is beginning organization of the exudate. The walls are thickened by newly formed granulation tissue, but the lesions are less pronounced than in the former block. The collapsed alveoli have thickened walls and in places there are also organizing fibrinous plugs. A few infundibula filled with pus and showing necrosis of their walls, are present. *Myocardium and kidney:* Normal. *Testis:* Interstitial fibrosis, and absence of spermatogenesis.

NOTE.—There is beautiful organizing bronchiolitis and peribronchiolitis, which may or may not be the late result of gassing. There is an indefinite history of "gas burns about eyes," and subsequent information indicates an exposure to yellow and blue cross shell, three and one half weeks before death. The data are too incomplete to warrant extended discussion and it is not altogether certain that the respiratory lesions are effects of the gassing.

CASE 93.—E. K., 2397299, Pvt., Co. G, 30th Inf. Died, September 4, 1918, at 9 p. m., at Base Hospital No. 27. Autopsy No. 46, performed on following day, by Capt. H. H. Permar, M. C.

Clinical data.—Gassed with mustard gas on August 10. Admitted to Field Hospital No. 110 on same day, and to Base Hospital No. 27 on August 12. Placed in diphtheria ward as suspect. Throat covered with gray exudate. September 4, throat culture positive for diphtheria bacilli. Extensive burns about whole body. General condition very bad.

Anatomical diagnosis.—Healing burns of skin of legs, thighs, buttocks, arms, genitals and axillæ, with pigmentation; diphtheritic pharyngitis, laryngitis, tracheitis and bronchitis; bronchopneumonia, acute, bilateral; edema and congestion of lungs; acute toxic myocarditis; acute lymphadenitis or peribronchial lymph nodes.

Microscopic examination.—There is an acute suppurative bronchitis, with complete necrosis of the mucosa, and acute inflammatory infiltration of the wall. Some of the smaller bronchi are completely plugged with fibrinopurulent exudate. There is no regeneration. The parenchyma shows patches of lobular pneumonia, emphysema and extreme alveolar edema in unconsolidated areas.

Bacteriological examination.—Smears of membrane taken post mortem shows diphtheria bacilli.

NOTE.—A case of mustard-gas poisoning, dying 25 days after exposure, with intense diphtheritic lesions of the upper respiratory passages, from which the diphtheria bacillus was cultured during life. The most unusual feature of the case is the absence of reparative changes in the bronchi and lungs.

CASE 94.—S. T., 490034, Pvt., Co. L. 47th Inf. Died, November 8, at 5 a. m., at Base Hospital No. 19. Autopsy No. 112, performed six and one-half hours after death, by Capt. H. H. Martland, M. C.

Clinical data.—Exposed to blue, green, and yellow cross shelling on October 13, near Verdun. Admitted to Gas Hospital No. 3 on same day, October 20, admitted to Base Hospital No. 76, with conjunctivitis, dermatitis of face and chest, laryngitis, and bronchopneumonia. October 24, patient very weak. Pulse 156. Temperature 99.8°. Respirations 28. Cough with large amount of expectoration. Severe conjunctivitis. Mucous râles over both sides of chest, especially left. October 24, admitted to Base Hospital No. 1. Severe bronchitis; no areas of consolidation found. October 27, membrane over uvula and soft palate. Culture positive for diphtheria bacilli. Diphtheria antitoxin, 6,000 units, given. October 28, admitted to Base Hospital No. 19. October 31, pulse rapid and weak. Eats very little. Dry skin. Raises large amount of purulent sputum. Moist râles, more numerous over left chest. Throat improving; 15,000 more units of antitoxin administered. Gradually growing weaker.

Summary of gross lesions.—No skin burns. There is extensive ulceration of the larynx, vocal cords, and trachea, which are covered with thick grayish membrane; this extends down to the finest bronchioles and is diffuse through both lungs. All lobes show a confluent bronchopneumonia. There is moderate distention of the chambers of the right heart.

Microscopic examination.—(a) There is gangrenous bronchitis which involves the entire bronchial wall and a zone of neighboring lung tissue. In the center of the gangrenous areas are large masses of bacteria. Elsewhere, the parenchyma shows a very widespread acute pneumonia, the exudate being rich in cells and fibrin. In some alveoli, there is beginning ingrowth of fibroblasts. Scattered through the consolidated lung are patches of necrosis with great numbers of bacteria. These are not always clearly related to the bronchi. (b) There is an organizing fibrinous pleurisy. In the lung tissue itself some of the bronchioles show a suppurative inflammation, with preservation of the epithelium; others gangrenous necrosis. There are emphysema and small patches of atelectasis. (c) The picture is a somewhat different one. There is almost complete collapse of the lung tissue, with extensive early organization in some areas, fibroblastic thickening of the alveolar septa, and edema. The bronchi are lined with regenerated metaplastic epithelium, resting upon a wall of highly vascular granulation tissue. In places the bronchi also are collapsed, the walls being practically intact, as seen in longitudinal sections. The arteries are surrounded by broad bands of edematous granulation tissue. (d) The section shows irregular areas of edema, emphysema, and moderate epithelial exfoliation. A small bronchus in the section shows an extraordinary obliterating process leading to practical closure of the lumen. The lining epithelial cells are curiously altered, and the basement membrane is hyalinized and thickened. There is a layer of granulation tissue between the mucosa and the circular muscle. (Fig. 37.) The process seems to be very like an obliterating endarteritis. That the stenosis of the terminal bronchi is the cause of the associated emphysema and atelectasis seems very probable.

NOTE.—Death 26 days after exposure to a mixture of suffocative and vesicant gases. The noteworthy features in the case are the gangrenous

bronchitis, with areas of necrosis in the parenchyma of the lung; the very extensive lobular pneumonia, showing in places, early organization; and the obliterating bronchiolitis in the nonpneumonic areas, associated with emphysema and areas of collapse. The recovery of the diphtheria bacillus from the membranous pharyngeal lesions is also of interest.

CASE 95.—E. S., 62768, Corpl., Co. 2, 101st Inf. Died, September 13, 1918, at Base Hospital No. 116. Autopsy No. 13. Autopsy, five hours after death, by Lieut. B. S. Kline, M. C.

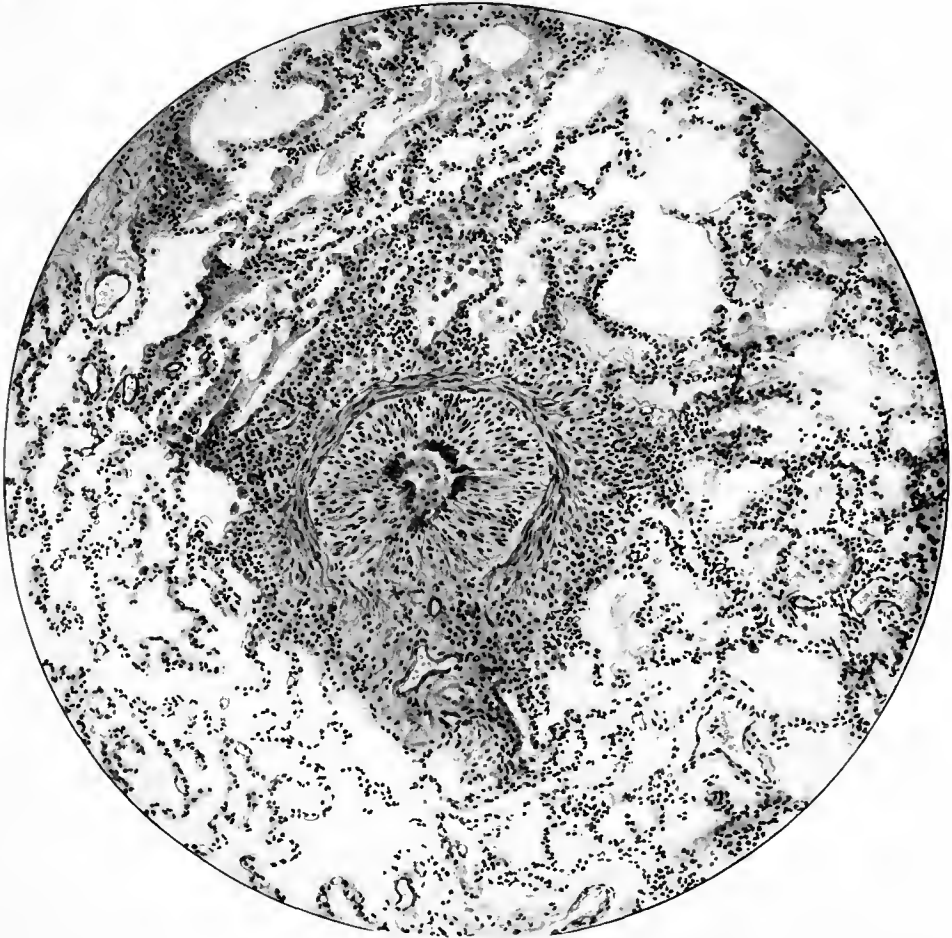


FIG. 37.—Case 94. Death, 26 days after exposure to mixture of suffocant and vesicant gases. Obliterative bronchiolitis

Clinical data.—Date of gassing, August 15. The patient was burned by the explosion of a mustard-gas shell above him while sleeping in a hayloft. Liquid covered his body. Admitted to Base Hospital No. 116 on July 24 with severe secondary burns involving entire back from neck down and including the buttocks and posterior surface of both thighs and back of legs. Burns also present on both arms, scrotum, penis, forehead, chest. Progressed fairly well with only moderate infection and superficial sloughing. Developed pressure necrosis over sacrum and both elbows, which grew steadily worse until death.

Anatomical diagnosis.—Extensive gas burns of skin of first and second degree, with secondary infection and moderate general brown pigmentation. Small areas of organized bronchopneumonia. Anemia and emaciation. Cloudy swelling of parenchymatous organs. Old vegetative endocarditis of mitral valve. Pulmonary edema.

External appearance.—The skin shows a striking picture. Beginning over the scapulae above, there is complete ulceration of the skin of the back as far down as the buttocks, where the posterior portion is likewise ulcerated. The ulceration continues down to the mid-portion of the thighs. Over the sacrum there is a large deep ulcerated area, in the base of which the sacrum and coccyx are visible. There is a moderate amount of viscid and caked exudate here. Above this deep wound there is a similar smaller wound over the crest of the ilium. The ulceration of the skin of the back, buttocks, and thighs extends well into the subcutaneous tissue. The base is covered by a moderate amount of foul-smelling sero-purulent exudate. In places there is dry scabbing. Ulcerations, similar in character but less extensive, are present over the posterior aspects of the legs, about the elbows and the knees, the right ear, crest of the ilium anteriorly. There is also an extensive deep ulceration of the scrotum and the base of the penis. Here the infection is most marked. The skin in general has a dull grayish-brown cast. Associated with the burns there is a moderate desquamation. There is also desquamation at some distance from the ulcerated areas. In places the burns show considerable healing. This is especially true of the small burns over the right hip, lower abdomen, upper arms, and chest. The superficial glands moderately enlarged. *Scalp:* Over the vertex there is some thick matted desquamation. The skin at one place shows a contusion. *Eyes:* The eyeballs are sunken in the sockets. The left upper eyelid shows a large area of ecchymosis. The conjunctivæ, however, and the mucous membranes are pale. At the right corner of the mouth there is a small superficial ulcerated area, base clean.

Gross findings.—*Pleural cavities:* On opening the thorax a number of fairly dense fibrous adhesions are found in the right sac, binding the posterior portion of the upper and lower lobes to the chest wall. In the left chest likewise a number of fibrous bands found binding the lateral portions of the upper and lower lobes to the chest wall. On incising the pericardial sac there is considerably less fluid than average. The pericardium is delicate and pale. *Heart:* Weighs about 330 grams. The right auricle considerably dilated. The tricuspid ring admits three fingers. There is slight dilatation of the conus. The valvular endocardium, thin and delicate, except the mitral valve, which shows along the line of closure several vegetations tightly adherent to the underlying endocardium. In part the vegetations are covered by endocardium. The chordæ, however, are thin and delicate. The base of the aorta shows small soft yellow opaque patches in the intima. The coronary vessels, no abnormalities, except that the right one opens by two mouths. The left myocardium on section is paler than normal. The architecture not altogether regular. There are scattered grayish flecks here and there. The tissue has a boiled and slightly greasy appearance. *Right lung:* All lobes fairly voluminous, eushiony, and inelastic. The lower lobe slightly soggy in addition. The glands at the hilum somewhat enlarged, edematous, pulpy, and not injected. The vessels, no abnormalities. *Bronchi:* The mucosa is pale and smooth. In the lumen there is a small amount of frothy fluid. The upper lobe on section presents a pink surface. The air sacs contain a small amount of fluid. In the posterior portion there are numbers of grape seed-sized to pea-sized firm consolidated areas, grayish-red in color. The middle lobe is well aerated and pink throughout. There is extremely little fluid in the air sacs. The lower lobe on section presents a pink surface. There is a small amount of thin, frothy fluid in the air sacs. In this lobe also there are numerous reddish patches, associated with some of which there are firm reddish-gray small consolidated areas. *Left lung:* Both lobes voluminous, eushiony, and inelastic. The glands at the hilum, vessels, and bronchi similar to those on the right. On close inspection of the bronchi the mucosa appears exceedingly thin. On section the upper lobe in general similar to the right upper. The lower lobe in general similar to the right lower lobe. *Organs of neck:* Glands in the lower portion of the neck are not appreciably enlarged. *Thyroid:* Considerably smaller than normal. The tissue coherent, pale. There is little colloid in the acini. *Larynx and trachea:* Present an interesting picture. The mucosa is exceedingly thin, pale, except in the region of the epiglottis, where it is somewhat diffusely thickened, pale with injection of the vessels here and there. The lymphatic tissue in the pharynx and the upper esophagus adjoining the glottis somewhat enlarged, injected. *Tonsils:* Enlarged, but scarred. Crypts clean. *Liver:* Weighs 1,400 grams. *Adrenals:* Right adrenal shows digestion of the medulla in one portion, with considerable extravasation of the blood here. There is moderate loss of the yellow pigment. The left shows no digestion of the medulla, some diminution in the yellow

pigment. In places there are fine gray streaks in the cortex. *Kidneys:* Normal. *Alimentary tract:* There is perhaps slight thickening of the mucosa of the upper esophagus, pharynx, and base of tongue. The stomach contains about 75 c. c. of thin, bile-tinged contents. The mucosa pale. Duodenum, ileum, the mucosa somewhat bile-tinged. In the lower ileum there are scattered patches of injection of the mucosa. The Peyer's patches are flat here, somewhat pigmented. The solitary follicles in the cecum are flat, pigmented. There is some patchy injection of the mucosa of the cecum and ascending colon. In the rectum there is quite diffuse moderate injection of the mucosa. The tissue about the rectum is somewhat edematous. The mesenteric lymph glands are not appreciably enlarged.

Microscopic examination.—*Skin:* Section passes through ulcer covered by infected slough. There is no healing at the margin and very little granulation tissue at the base. The adjacent epithelium contains little pigment, but there are beautiful melanophores in the superficial layer of corium sending processes between the basal epidermal cells. Another block shows thinning of epidermis with hyperpigmentation. *Trachea:* Epithelium is intact and normal save for post-mortem desquamation. Epithelium is ciliated. There is no edema, congestion, or inflammatory infiltration of submucosa. No bacteria found in section. *Lungs:* Bronchi still have intact epithelium, but are filled with pus. Atria are dilated and their epithelium necrotic. There are patches of lobular pneumonia and interstitial infiltration. The exudate is cellular, not fibrinous. No organization. There are many pigmented exfoliated epithelial cells. Section stained with Gram-Weigert shows practically no bacteria or fibrin. *Kidneys:* A few of the glomerular tufts contain hyaline thrombi. No other changes. *Myocardium, spleen, and pancreas:* No abnormalities.

NOTE.—Mustard-gas case of 29 days' duration, with very extensive contact burns of skin. The respiratory lesions do not indicate gas inhalation. There was a terminal pneumonia in the lung which also showed signs of chronic passive congestion associated with the mitral lesions. Death in this case was primarily the result of very extensive skin burns associated with infection or toxemia.

CASE 96.—W. A. H., 2182677, Pvt., 354th Inf. Died, on September 7, at 7 a. m., at Base Hospital No. 42. Autopsy No. 3, performed three hours after death, by Capt. F. A. Evans, M. C.

Clinical data: Gassed on August 8, near Toul, with mustard-gas shells. August 10, admitted to Base Hospital No. 42. August 20, the patient began to have a temperature of 100° to 101°, followed a few days later by areas of bronchovesicular breathing front and back. There was a definite area of consolidation, especially marked in the angle of the right scapula. For a few days the patient improved and did very well. August 28, scattered râles over upper front on both sides, with bronchovesicular breathing over lower right anterior chest. There was a click on expiration and inspiration over this area. In the back, various kinds of râles were heard on both sides; impairment of resonance over lower right side, beginning about 5 cm. below the angle of the scapula. September 4, signs of irregular consolidation over entire right lower lobe, and also over right upper chest anteriorly. The patient, from this time on, became more intoxicated; breathing became labored; there was very abundant purulent sputum. September 6, condition very bad. Laryngoscopy on August 30 showed the vocal cords covered with a film of mucopurulent exudate. Died on September 7, at 7 a. m.

Anatomical diagnosis.—Acute tracheitis and bronchitis; bronchopneumonia of all lobes; acute fibrinous pleurisy; healed mustard-gas burns of axillæ; perineal region, buttocks, and popliteal spaces.

External appearance.—Few superficial excoriations under the lower lip. There is pigmentation of healing gas burns in the perineal region over the inner and posterior aspects of the thighs, over the buttocks, and popliteal spaces. Similar but less pronounced pigmentation is seen in the axillæ. There is purulent exudate in both eyes.

Gross findings.—*Right lung:* Floats in water and is voluminous. In certain areas, notably at the extreme apex of the upper lobe and the extreme base of the lower, posteriorly, the lung tissue appears normal. There is fibrinous deposit over the lower surface of the upper lobe, over the middle lobe posteriorly, and over the upper part of the lower lobe. There is also a heavy deposit of fibrin in the interlobar fissures. Those places that have not been

described as normal have a pinkish-purple color and on palpation are in part air containing, in part consolidated. There is an isolated area of dark color in the posterior part of the upper lobe extending from the fissure to the apex, which has a nodular feel. On section, there is an irregular and patchy bronchopneumonia. The lung tissue is everywhere moist and, where not consolidated, of a salmon-pink color, from which the small bronchopneumonic nodules stand out. The larger bronchi of the right lung are injected, and pus exudes from them on cutting. *Left lung:* Also is voluminous. There is a fine fibrinous pleural exudate most marked posteriorly. On section, the lung tissue is less moist than that of the right lung; it is spotted with areas of bronchopneumonia, varying in size from miliary to that of a bean. The pneumonic consolidation is most extensive in the posterior part of the lower lobe. The larger bronchi are injected, but their mucosa appears to be intact. *Organs of neck:* Larynx and pharynx are normal. *Trachea:* Shows a fibrinomucopurulent exudate, which when stripped off shows the underlying mucosa intact and only moderately congested. No scarring is apparent. *Heart* normal. *Intestines* not removed. Remaining organs show no significant changes.

Microscopic examination.—*Trachea:* Epithelium is everywhere intact, but resembles esophageal epithelium, being squamous and nonciliated. The same alteration is present in the epithelium lining the mucous ducts. The glandular acini are distended with mucus. The submucous tissue is evenly infiltrated with wandering cells having stained distorted nuclei. The preservation of the tissue is too poor to identify these with certainty. Most of them appear to be lymphoid cells. The capillaries are wide, but contain no preserved red blood cells. *Lungs:* The smaller bronchi are wide, their walls thickened by granulation tissue and closely invaded by leucocytes. Some are lined by a thin layer of flattened epithelial cells; in others the rough granulation tissue lies exposed. Many of them contain purulent exudate, and most of the terminal bronchioles and infundibula are filled with it. The adjacent lung tissue over a narrow zone shows an organizing pneumonia. A second block shows an extensive bronchopneumonia, which is not of the usual influenzal type, inasmuch as the exudate is very cellular. The leucocytes are well preserved, and the process seems of recent date. A third block shows an organizing bronchiolitis, with plugs of vascularized tissue growing from the walls. The smaller bronchi are greatly thickened by new formed granulation tissue and surrounded by zones of edema. *Liver, spleen, myocardium, and adrenal* show no features of special interest.

NOTE.—A case of mustard-gas poisoning, dying 30 days after exposure. There were healing burns in characteristic situations at autopsy, and histological examination shows the typical metaplasia of the tracheal epithelium and subacute bronchitis and peribronchitis similar to that seen in other mustard-gas cases after the lapse of several weeks. In addition, however, there appears to have been a lobular pneumonia of more recent date.

CASE 97.—T. F. (Cherokee Indian), 48537, Pvt., Co. M, 18th Inf. Died, November 6, 1918, 9.20 a. m., at Base Hospital No. 58. Autopsy No. 17. Autopsy, four hours after death, by Capt. M. Flexner, M. C.

Clinical data.—Exposed to phosgene and mustard-gas shells on October 1, near Charpentery. Admitted to Base Hospital No. 58, October 15, with severe cough and pain in chest. Diagnosis: Bronchopneumonia, with suspicion of lung abscesses.

Anatomical diagnosis.—Mustard-gas burns, healing at left wrist, hemorrhagic and gangrenous tracheitis, bronchitis, and bronchiolitis. Extensive peribronchial pneumonia. Chronic fibrous pleurisy. Parenchymatous degeneration of liver and spleen.

External appearance.—Body is that of an Indian. The skin is brownish-tan in color, with darker pigmentation over abdomen and thighs, almost white over lower legs and feet. Over end of radius on left wrist is a healing burn circular in shape, with slight scab formation at lower edge. Over coccyx is a beginning ulcer.

Gross findings.—*Pleural cavities:* The left is obliterated by old adhesions. The right is free from fluid or adhesions. *Heart:* Normal. (Note dictated upon receipt of organs at pathological laboratory, experimental gas field.) *Right lung:* Pleura over upper and lower lobes is normal. Over the lower lobe are the remains of old fibrinous adhesions. Posterior half of lung is dark with sunken patches of collapse. The anterior portion is pale and

emphysematous. *Bronchi*: As far as can be followed, are lined with dark greenish-brown mucosa, contain a little dark, foul-smelling exudate. No diphtheritic membrane. On section, the upper lobe, in the posterior portion shows numerous discrete yellow foci surrounded by irregular patches of hemorrhagic consolidation. These areas correspond to the cross section of small bronchi dilated with plugs of exudate. Same condition throughout the lower lobe, with exception of small patches anteriorly. The consolidation, however, is more widespread and the intervening lung tissue less well aerated. The middle lobe, with the exception of the extreme anterior strip, is air-containing and dry. The bronchial lymph nodes are small and pigmented. Large branches of the pulmonary artery are normal. *Left lung*: Both lobes are covered with sheetlike adhesions. The apex is deformed by old scars. Several calcified nodules in the substance of the lung can be felt about one inch below the extreme apex. Upper lobe on section is air-containing. Along the posterior border the walls of the bronchi show greenish-brown discoloration. The lower lobe is very dark in color, firm and nodular. Numerous foci of grayish-yellow project upon a background of dark red, uniformly consolidated. On pressure plugs of dense exudate can be expressed. Section shows also small irregular cavities with necrotic walls, and representing small dilated bronchioles. The bronchi show the same intense hemorrhagic condition as in the right lung. The fetid odor is apparently not due to post-mortem change. *Trachea and bronchi*: Are markedly injected with blackish-gray discoloration of the wall. There are small yellow flecks in the contained secretion. *Gastrointestinal tract* is grossly normal. Remaining organs show no significant lesions.

Microscopic examination.—*Trachea*: The mucous membrane in places is preserved, and the lining epithelium is not atypical, showing well preserved cilia. Desquamation is probably post mortem, since there is no edema of the corium, no membrane formation, no inflammatory infiltration and no evidence of regeneration. *Lungs*: Bronchioles show necrosis. There is complete loss of epithelium without formation of membrane or exudation of leucocytes into the lumina. In many places the peribronchiolar tissue is involved in the necrosis. Only faint indications of alveolar outlines persist. Detritus, which lines these gangrenous cavities, is very rich in organisms. The necrotic areas are surrounded by a zone of bronchopneumonia with many polymorphonuclear leucocytes in the exudate. External to these the alveoli contain much fibrin. In some areas these peribronchial pneumonic patches are undergoing organization. There is much edema about the large vessels with formation of abundant young connective tissue. Septa also are edematous and in places organized and contain many lymphoid and plasma cells. *Skin*: Superficial desquamation of the keratin layer, slight edema of corium with a few wandering cells. No other significant lesions. Section of kidney, pancreas, spleen, and myocardium show no changes of interest. *Liver*: Shows rather marked periportal fat infiltration.

NOTE.—Exposed to phosgene and mustard gas 37 days before death. There was a healing mustard-gas (?) burn of the left wrist, but no other cutaneous lesions suggestive of previous gassing. Findings in the trachea were not indicative, but there was a gangrenous bronchiolitis associated with a widespread hemorrhagic bronchopneumonia, which was becoming organized. While it is probably a late mustard-gas case, it is difficult to make a differential diagnosis from influenzal pneumonia complicated by a gangrenous bronchiolitis. A point of interest in this case is the presence of obsolete apical tubercles, which after 35 days have not become activated.

CASE 98.—C. M., 17004, Pvt., 2 Northumberland Fusiliers. Died, November 12, 1918, at 1 p. m., at Base Hospital No. 2. Autopsy, five hours after death, by Capt. B. F. Weems, M. C.

Clinical data.—October 5, admitted to No. 20 Casualty Clearing Station. *Diagnosis*: Gas-shell wound of left thigh, right foot, left hand; gassed. *Operation*: Amputation of left thigh, right foot. Left hand cleaned up. Patient's condition very poor. Blood transfusion. October 7, admitted to Base Hospital No. 2. Stump of left thigh fairly clean, right foot very dirty, completely excised and part of first and second metatarsals removed; posterior tibial vessels tied; not amputated because of amputation of opposite thigh. Wound of left hand very dirty. Fifth finger amputated. Corneal ulcer of left eye. October 28, has

been doing only fairly well; foot still badly infected. Incision on dorsum to-day; abscess apparently arising from tarsal joints. November 5, patient doing poorly; running temperature of 103° and 104°. Blood culture sterile; moderate generalized bronchitis; has apparently an infection of most of the tarsal joints. Amputation through junction of middle and lower third of right leg under stovaine intraspinally. Transfusion 700 c. c. Stood operation well. November 12, condition has grown steadily worse. All wounds appear clean. Many fine râles at both bases with much cough. Died at 1 p. m.

Anatomical diagnosis.—Acute membranoulcerative laryngitis, tracheitis and bronchitis; bronchopneumonia; edema and congestion of both lungs; multiple abscesses, both lungs; acute fibrinous pleurisy, amputation wounds of both legs, and finger of left hand; emaciation; poisoning with irritant gas.

External appearance.—Much emaciated; adenoid facies; many teeth missing. Skin and external genitals normal. Wounds as follows: Left-hand middle finger missing; ulcerated, partially healed wound over area of amputation; left leg amputated in mid thigh; stump apparently clean; right leg amputated just above foot; upon removing sutures, tissues are found to be clean and apparently healing.

Gross findings.—*Pleural cavities:* Lungs are collapsed to some extent; there are about 100 c. c. of fluid in the left pleural space; loose fibrinous exudate and fluid over the entire posterior surface and base of right lung. *Left lung:* Moderately voluminous; there is a slight amount of fibrinous exudate over posterior surface; lower portion of upper lobe, as well as greater portion of lower lobe, is consolidated. *Bronchi:* Contain slightly purulent and sanguineous exudate; mucous membrane is much eroded and covered by exudate. Upon section, the lung presents a dark grayish-red color; the surface is moderately smooth, exuding a large quantity of serum and blood; there are numerous small points of pus over the surface. It is rather a diffuse type of lobular pneumonia combined with edema. *Right lung:* Covered with thick fibrinous exudate. The lower lobe and a large part of the upper and middle lobes are of rather firm and lumpy consistence. The lung upon section reveals much the same picture as the left. There is a diffuse partial consolidation, roughly lobular in type. The bronchi are filled with pus and necrotic membrane; many small abscesses are present at the end of the bronchi. Edema is pronounced. The glands at the hilum are much enlarged. *Organs of neck:* *Tonsils* normal. *Epiglottis:* Tremendously thickened and covered by a yellowish-gray membrane; the mucosa is eroded. The arytenoepiglottic folds are also much thickened and ulcerated. *Trachea:* Is covered over its entire length by a thick cheesy membrane, beneath which the mucous membrane is deeply ulcerated. *Heart* normal. *Gastrointestinal tract:* Not recorded. Remaining viscera show no significant changes.

Microscopic examination.—*Epiglottis:* On both sides a diphtheritic necrosis extending almost to cartilage. Much fibrin is present, both on the surface and in the edematous submucous tissue. There is hyperemia and hemorrhage. Many of the small vessels contain thrombi, some of which are becoming organized. There are many mononuclear and polymorphonuclear leucocytes loosely scattered through the tissues; they appear pyknotic. The cartilage also is affected, showing in places fibrillary degeneration of the ground substance, with swelling and loss of definition of the cartilage cells themselves. *Trachea:* There is a thick adherent membrane, densely crowded in places with fragmented and pyknotic leucocytes; on the surface of this is a loose purulent exudate containing masses of Gram-positive cocci. There is no epithelium remaining. The submucosa shows numerous fibroblasts, pyknotic leucocytes, and congested vessels. The mucous ducts are wide and filled with exfoliated cells. *Lungs:* A bronchus cut longitudinally is practically filled with a thick fibrinous plug in which are many pigment-containing cells, and a few ingrowing fibroblasts. The alveoli everywhere contain plugs of loose fibrinous exudate, poor in cells, which are continuous with similar plugs in the distended atria. Few large mononuclear cells and polymorphonuclears and isolated spindle cells are present in the fibrin. The septa are thickened and loose in texture and under the high power the epithelium is frequently found elevated from the capillaries in a continuous sheet, presumably by edema. There are occasional hemorrhagic extravasations between epithelium and blood vessel, or into the alveolus itself. The epithelial cells, judging by their swollen contours and dark staining protoplasm, are probably in large part new formed, although no mitoses are found. Another block of lung tissue shows in general the same picture. There is fibrin upon the surface of the pleura, which is exceedingly edematous. In its basal portion are many congested blood vessels with fresh hemor-

rhages. Beneath the pleura in one place is an abscess about 2 mm. in diameter. The lymphatics in the interlobular septa are distended with masses of degenerating leucocytes. Liver, spleen, adrenal, and kidney show nothing abnormal.

Bacteriological examination.—Blood culture (post-mortem) staphylococcus albus. Culture from bronchus: *B. influenzae*, streptococcus hemolyticus, staphylococcus aureus, Gram-positive diphtheroid bacillus. Culture from bronchiole, staphylococcus aureus. Culture from pleura: Staphylococcus aureus. Culture from lung: *B. influenzae*, diphtheroid bacillus.

NOTE.—History of gassing, 38 days before death, with severe wounds of lower extremities, later necessitating double amputation. There is no record of skin burns, and none are described in the autopsy protocol. There is said to have been a corneal ulcer, but there is no mention of conjunctivitis. The upper respiratory tract showed a membranous necrosis of great severity, with complete epithelial destruction. Repair was therefore limited to attempted organization in the deeper tissue, but was very imperfect. The small bronchi still contained plugs of dense exudate, which was undergoing early organization. There was a lobular pneumonia which also showed evidence of organization and epithelial repair. There were a few suppurative foci. Presumably, the case is one of mustard gas inhalation, in which, as in other autopsies at this hospital during the same period, the cutaneous lesions are slight or absent. The surgical complications, in this case, though very grave, can not be regarded as the cause of death.

CASE 99.—J. Y., 105587, 16th Inf. Died, November 10, 1918, at 7 p. m. Autopsy, 14½ hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—October 2, admitted to Field Hospital No. 12 with shell wound of right side. Foreign body about 6 mm. long beneath superficial muscles of right chest. October 4, multiple burns of skin, dressed with vaseline each day. October 24, incision and drainage of large abscess of right buttock. October 25, patient complained of difficulty in opening jaw; no stiffness of neck. November 1, incision of gluteal abscess and inguinal glands. Antitetanic serum 5,000 units intraspinally, 10,000 intramuscularly. November 2, fluoroscopic examination showed foreign body, 1 by 1 cm. lying 10 cm. under skin apparently in the body of the liver. November 3, subdiaphragmatic abscess; operation; resection of rib and evacuation of abscess. Culture of pus showed anaerobic Gram-positive bacilli and Gram-positive diplococci. Forty thousand units of antitetanic serum intramuscularly. November 10, the patient grew rapidly worse, although tetanus was cured. Frequent vomiting, incontinence of feces, much thick sputum, and definite signs of peritonitis. The patient died, November 10 at 7 p. m.

Anatomical diagnosis.—Gunshot wound of abdomen, with perforation and laceration of liver (encapsulated bit of shrapnel, with clothing fragments and small spicules of bone), subsequent infection, abscess formation; thrombosis, local hepatic veins; small infarct, left upper lobe; subdiaphragmatic abscess; local organizing peritonitis; resection of seventh rib, right; drainage of liver abscess and abscess of right buttock; surgical incisions and drainage; decubital ulcer over sacrum, beginning healing; healing extensive superficial gas burns of skin, with moderate general brown pigmentation, and considerable local brown pigmentation of trunk, extremities, and scalp; anemia and marked emaciation; healing and acute purulent bronchitis; areas of bronchiectasis; old peribronchial and peribronchiolar pneumonia of all lobes except right middle; recent bronchopneumonia, right upper and lower lobes; fibrinopurulent pleurisy, right; acute splenic tumor; cardiac dilatation, right (slight); pulmonary edema (slight).

A detailed autopsy protocol of this case was not made, owing to stress of other work (personal communication from Lieut. B. S. Kline).

Microscopic examination.—*Large bronchus:* Presents no clear evidence of previous gas injury. The epithelium is defective in places, but this is probably due to postmortal desquamation. Where it is still intact, it is ciliated, and in no wise abnormal. The subepithelial tissue contains pink-staining hyaline material, which is probably old fibrin. The blood

vessels are congested. There are moderate numbers of lymphoid cells. The mucous glands are normal. *Lungs*: (a) Section shows an acute confluent bronchopneumonia, presenting no special features. There are no other lesions indicative of previous gassing. (b) In addition to patches of acute bronchopneumonia, the bronchioles show changes which are probably of older date, and may be referable to gas inhalation. Some are dilated and contain fibrinopurulent exudate which in places is becoming organized; the walls are formed by a hyperemic granulation tissue, densely infiltrated with round cells and plasma cells. The epithelium in some is ciliated; in others, flat and atypical; in still others, lost. The adjacent alveoli are collapsed and compressed, and there is hemorrhage and fibrinous exudate, showing early organization. Irregular nests of proliferated epithelium fill up some of the alveoli. (c) The section shows an old infarct, at the apex of which is an organizing thrombus, already well canalized. In the noninfarcted area the bronchioles and infundibula show lesions similar to those in (b) and probably due to the original gassing. *Liver*: Section shows healing scars with granulation tissue and much foreign material on surface. *Spleen*: Fragmentation of cells in centers of follicles, marked congestion of pulp, and much pigment deposit. *Kidney*: Acute degenerative changes in epithelium of convoluted tubules.

NOTE.—There is a definite clinical history of old mustard-gas burns, and healing and pigmented burns were present at the autopsy 39 days after the injury was incurred. The pulmonary lesions were complicated by the presence of an infarct, doubtless due to an embolus from the hepatic veins, and by a terminal bronchopneumonia complicating the abdominal injuries. There were, nevertheless, traces of old respiratory burns in the small bronchi and infundibula, although the larger bronchi showed restitution of the epithelium.

CASE 100.—R. A. B., 2181649, Corpl., 355th Inf. Died, September 28, 1918, at 12.40 p. m., at Base Hospital No. 116. Autopsy, three hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—August 10, admitted to Base Hospital No. 116, suffering from mustard-gas inhalation and contact received in action on August 8. Said to have been exposed to yellow and green and blue cross shells for six hours. There were on admission extensive body burns, conjunctivitis, laryngitis, and bronchitis. August 12, consolidation of right lower lobe. August 20, scattered areas of consolidation over both lungs, with complete consolidation of left lower. September 10, diarrhea. September 15, signs of fluid at the base of the left lung. Aspiration showed pus. September 16, operation for empyema. Since admission there has been gradual emaciation which is now very marked. The gas burn of the lower back has never healed, and has become a bed sore. The right lung presents harsh breathing and many coarse, moist, bubbling râles. Diagnosis: Bronchiectasis, with purulent expectoration. Died, September 28 at 12.40 p. m.

Anatomical diagnosis.—Healed gas burns, upper respiratory tract and skin; diffuse and local brown pigmentation of skin; organized bronchopneumonia, left lower lobe; empyema, left; resection of portion of ninth rib; extensive organizing fibrinopurulent pleurisy, left; dilatation of bronchial branches, slight; purulent bronchitis, slight atelectasis of left lung, moderate; compensatory emphysema, right lung; rupture of thoracic aorta, false aneurysmal sac; old tuberculous foci, right lower lobe; healed pleural adhesions, right; decubital ulcer of sacrum, healing; anemia and emaciation, marked.

External appearance.—Body markedly emaciated and anemic; slight hypostasis. The skin in general has a slight brownish tint. Scattered over the thighs, genital folds, lower abdomen, elbows and upper arms, there are irregular blotchy areas of deeper brown pigmentation. In some of these, the epidermis is desquamated in the inner portion. The outer surfaces of both thighs and the scrotum show thin pearly areas several centimeters in diameter. Over the sacrum posteriorly, there is an area of ulceration 4.5 cm. extending into the muscles; the base clean, showing healing. The skin edges show new epidermis. Operative wound below angle of left scapula, with drainage into pleural cavity.

Gross findings.—*Pleural cavities*: On opening the thorax, a small number of fibrous bands found in the posterior and inferior portions of the sac on the right side. On the left both lobes collapsed against the spine. There is a large air space present, with firm adhesions over the upper and lower lobes posteriorly. In the sac are a few pockets of viscid pus. The heart is displaced somewhat to the right. Its long axis is parallel to the long axis of the

body. The pericardial sac on the left is bound to the lung by firm bands; otherwise pericardium is normal. *Right lung:* All lobes fairly voluminous, cushiony, inelastic. The pleura thin; the vessels present no abnormalities. The glands at the hilum are intensely pigmented and scarred. The bronchial mucosa is pale, perhaps slightly thickened. On section of all lobes, a light pink very well aerated surface presents. The upper portion of the lower lobe shows a scarred pigmented patch 2 by 1.5 cm., embedded in which there are firm whitish-yellow nodules. On this side, some of the bronchial branches contain viscid mucopurulent secretion; and in addition in places peripherally are moderately dilated. *Left lung:* Both lobes considerably collapsed. The pleura diffusely thickened, covered by tenacious fibrinopurulent exudate, which when stripped shows tiny vessels between it and the pleura. The pleura itself is diffusely injected. The vessels and glands are similar to those on the right side. The bronchi show slight patchy injection of the mucosa. In the lumen there is thin viscid fluid. On section of the upper lobe, a light pink well aerated surface presents. In the posterior portion, there is a firm gray area 1.5 cm. in diameter, suggesting organizing pneumonia. No consolidation elsewhere. The lower lobe on section presents a similar picture to the upper, except that it is not consolidated. In both lobes some of the peripheral bronchial branches show moderate dilatation. In the lumen, there is viscid mucopurulent material. Between upper and lower lobes posteriorly there is a mass of soft purulent exudate. Encapsulated in the inferior portion of the lower lobe, there is a small amount of viscid pus similar to that in the surgical wound described above. Scattered through the left lower lobe are numerous tiny nodules suggesting organizing pneumonia. In this lobe also a number of the medium-sized bronchioles are somewhat dilated. *Organs of neck.—Trachea and larynx:* Mucosa pale, perhaps slightly thickened. There is no outspoken evidence of former inflammation. *Tonsils:* Small and scarred. *Heart:* Brown atrophy, not otherwise abnormal. *Aorta:* Moderate atherosclerosis with rupture at junction of transverse and descending portions of arch, and false aneurysm formation. *Gastro-intestinal tract:* Patchy injection, but no other significant changes. Remaining viscera show no lesions of interest.

Microscopic examination.—Skin: Area from which specimen was taken is not known, possibly scrotum, because of abundant large sebaceous glands and corrugated surface. There are few definite alterations. The stratum corneum is loose and partially exfoliated. There is an excessive amount of pigment in some areas of the stratum mucosum, and rather numerous branching chromatophores in the superficial layer of the corium. There are no inflammatory changes, and the appendages are normal. The superficial vessels are collapsed and not thrombosed. In a few areas there is irregular arrangement of the epidermal cells with considerable hyperkeratosis. *Trachea:* Epithelium over the greater portion of the section is of the normal stratified ciliated type. The arrangement of the cells is orderly and there is nothing to indicate a previous injury. In one area, however, there is a superficial ulcer, where the epithelium is defective, and the base formed by dense scar tissue, in which the connective tissue cells have dense distorted nuclei. The subepithelial tissue is loose and contains many scattered wandering cells, predominantly plasma cells. There are also large mononuclear elements, fibroblasts, and phagocytes filled with hemosiderin pigment. These cells, especially lymphoid and plasma cells, are present in numbers between the acini of the mucous glands. *Lungs:* There is dense organizing fibrinous exudate on the pleura, 2 mm. in thickness. The underlying tissue is collapsed, the septa thickened. There are well-organized plugs, with new-formed blood vessels and many pigment cells in some of the bronchi (see fig. 25) and alveoli. Here and there are dense masses of fibrin still present in the alveoli. These are invaded by scattered connective tissue cells, and covered often by flattened epithelium. Others are filled with vacuolated fat-containing epithelial cells. The interlobular septa are edematous, but organization is in progress. *Myocardium, spleen, liver, and adrenals:* No significant changes.

NOTE.—Death 51 days after exposure to mixed suffocant and vesicant gases. Death probably due to empyema, complicating the gas pneumonia. The trachea showed localized ulcers, but over large areas there is complete regeneration of ciliated epithelium, a point of great interest since it indicates that the squamous metaplasia is not a permanent nor inevitable effect of the gassing. The organizing bronchiolitis is also of interest.

CASE 101.—C. D., No. —, Pvt., 28th Inf. Died, November 21 at 5 p. m., at Base Hospital No. 116. Autopsy, 16½ hours after death, by Lieut. E. S. Maxwell, M. C.

Clinical data.—October 2, admitted to Base Hospital No. 23. Diagnosis: Mustard-gas poisoning. Held for mental observation. October 27 transferred to Base Hospital No. 116. Eyes and head generally burned. Scattered râles in lungs. The patient is extremely active with intent of destruction, and requires restraint. Apparent mania due to toxic and exhausted state. November 5, leucocytes 18,200. The patient's condition mentally and physically is worse. Irregular temperature, at times reaching 104°. An area of dullness has developed over left lower and lower part of left upper lobes. No fluid obtained on tapping chest. November 21, respirations rapid and shallow, pulse feeble and irregular. Pulmonary edema and cardiac exhaustion. Died at 5 p. m.

Anatomical diagnosis.—Gas burns, mustard gas (slight): Healed tracheitis and suppurative bronchitis; organizing coalescing lobular pneumonia, left upper and lower lobes; peribronchial pneumonia, right upper lobe; fibrinopurulent pleurisy, bilateral (600 c. c. left, 200 c. c. right); acute lymphadenitis; regional lymph nodes; pulmonary edema, moderate; cardiac dilatation, right (moderate).

Detailed autopsy protocol not received.

Microscopic examination.—*Trachea and large bronchus:* No material preserved. *Lungs:* Pleura covered with thick fibrinopurulent exudate, which is evidently very recent since there is no organization in progress. There are no larger bronchi included in the section. The bronchioli are filled with purulent exudate, and their epithelia invaded by leucocytes. There is no necrosis or membrane formation. The most striking feature is a diffuse alveolar edema, partly fibrinous, in which are seen a few pigmented epithelial cells but very few leucocytes. Occasionally there are some spindle-shaped fibroblasts, but the organization is not widespread and is extremely early. There is edema also about the arteries and veins; the lymphatic spaces are widely distended with plugs of purulent exudate, which in places simulate small abscesses. *Bronchial lymph nodes:* Show no features of special interest.

NOTE.—There is a definite history of mustard-gas intoxication, with typical burns and very severe mental symptoms. The injury was received approximately 52 days before death. The pulmonary symptoms appear to have been of later development, and it is difficult to ascribe the histological lesions found in the lungs to the initial injury. The material is defective, no tissue from the trachea or larger bronchi having been preserved.

CASE 102.—A. K., 2181274, Corpl., Co. A, 355th Inf. Died, October 1, 1918, at 7.45 a. m., at Base Hospital No. 18. Autopsy No. 100, performed eight hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—None available. There were numerous casualties from gas on August 7 and 8, on which days Co. A of the 355th Infantry was exposed to severe shelling with yellow, blue, and green cross shells. In all probability this is the correct date of gassing.

Anatomical diagnosis.—Gas burns of respiratory tract, with healing in larynx and trachea; intense bronchitis; extensive peribronchial pneumonia of all lobes except right middle, in large part organizing; multiple abscess formation, left lower lobe; localized areas of gangrene, left lower lobe; extensive recent lobular pneumonia; organizing fibrinous pleurisy, left lower lobe, slight; acute lymphadenitis of regional lymph nodes; slight general brown pigmentation of skin; anemia and emaciation marked.

External appearance.—The skin in general has a dull light brownish cast, most marked in the folds and over the lower abdomen. *Eyes* normal. *External genitalia* normal.

Gross findings.—*Pleural cavities:* Fibrous bands over the upper lobe on the right side, and a small amount of fibrinous exudate on the left. *Right lung:* Is voluminous and cushiony; the upper lobe shows solid patches posteriorly; the middle lobe is well aerated; the lower lobe is like the upper. The glands at the hilus are greatly enlarged, pulpy, edematous, somewhat injected. The vessels are normal. The bronchus shows marked injection and hemorrhage into the mucosa. In the lumen there is thin, viscid, green-tinged fluid. The bronchial cartilages cut with more than usual resistance. On section of the upper lobe, the posterior half shows patchy consolidation, the cut surface in the pneumonic areas being pinkish-gray to yellow. In places the consolidation is soft, coherent, pulpy, and yellowish.

The finer bronchioles contain viscid pus. The larger bronchi show considerable thickening of their mucosa. Mesially, the tissue is well aerated and pink. The consolidation is in great part peribronchial; in places it is firm and gray, suggesting organization. The middle lobe on section is pink and air-containing. The bronchioles contain viscid purulent material. About some of them there is a small amount of pinkish-gray consolidation. The lower lobe is strikingly less affected than the upper, but presents in general a similar picture. The bronchial thickening and peribronchial consolidation are even more conspicuous. In addition, the bronchioli show slight but definite diffuse dilatation. This is especially marked at the periphery of the lobe, where the bronchioles are equal in size to ordinary good-sized bronchial branches. *Left lung:* The lower lobe is much more voluminous than average and in great part soggy. The upper lobe is of average volume. Over the lower lobe, tightly adherent, apparently organizing fibrinous exudate in small amount is present. The glands at the hilum, vessels, and bronchi similar to those on the right side. On section the upper lobe is aerated and pink in its upper portion; in the lower portion, especially posteriorly, there are numerous areas of consolidation similar in appearance to those on the right and associated with the bronchial branches. The lower lobe on section presents a striking picture. The consolidation involves the greater portion of the lobe. There are softened areas in the consolidated regions in many places. There is a dull-grayish appearance in the cavities and neighboring edematous lung. The odor is characteristically gastric. In the relatively uninvolved portions of the lobe there is considerable edema. In places, this has a yellowish tinge, suggesting much fat. The picture in this lobe is that of extensive peribronchial and lobular consolidation, with multiple areas of softening and abscess formation and considerable edema. *Organs of neck—Larynx:* Shows prominent streaky gray thickening of the mucosa. *Trachea:* Shows similar gray streaking and uniform thickening of the mucosa, also considerable old diffuse hemorrhage. *Tonsils:* Slightly enlarged and on the right there is a large crypt containing milky fluid. *Heart:* Normal, except for brown atrophy. *Gastrointestinal tract:* No significant changes. Remaining viscera show no lesions of interest.

Microscopic examination—Trachea: The lining is constituted by a rather dense granulation tissue which is devoid of epithelial covering, save for a few small islands of layered, nonciliated cells. There is a fairly profuse inflammatory infiltration; many of the cells show distorted nuclei and are difficult to identify. The mucous glands are atrophic, the few remaining acini being surrounded by dense accumulations of lymphoid and plasma cells. Some of the glandular cells show an interesting metaplasia into solid nests of squamous cells, like islands of carcinoma cells. The adjacent lymph nodes show areas of fibrosis. There is much scar tissue about the cartilage. *Large bronchus:* The epithelial lining is desquamated, save for a single row of adherent cells. In a few places, where the cells are still attached, they are seen to be arranged in an orderly way and to be distinctly ciliated. The submucous tissue has the character of a loose granulation tissue with many wide, thin-walled, blood vessels. There is dense cellular infiltration, composed largely of plasma cells. The mucous glands are atrophic and surrounded by fibrous tissue and inflammatory cells. The lumen of the bronchus contains bacteria and leucocytes, with exfoliated epithelial cells. *Lungs:* (a) The bronchi are represented by abscesslike masses of pus and bacteria, surrounded by granulation tissue which is very vascular and thickly infiltrated with lymphoid and plasma cells. Very few of these suppurative bronchi show remains of an epithelial lining, but in a few of them shreds of adherent, flattened, regenerating cells serve to identify these structures as dilated and infected bronchi. The dilatation is proven by compression of the adjoining alveolar spaces. The parenchyma is almost uniformly consolidated, but the alveolar contents vary. Many of the alveoli are filled with a homogeneous, granular or fibrinous coagulum; others contain in addition large, rounded, foamy, and apparently fat or lipoid containing epithelial cells. In some areas, especially about the bronchiolar abscesses, the alveolar exudate is undergoing organization; pale spindle cells invade the coagulum. The septa are cellular and thickened; there is an increased number of nuclei belonging chiefly to lymphoid cells. The alveolar capillaries are not congested. The alveolar epithelium in many places is actively regenerating, as shown by the deep staining and cylindrical shape of the cells. The pleura is smooth; the subpleural capillaries are wide and congested. The lymphatics also are dilated and filled with homogeneous coagulum. (b) In general, a similar picture. One bronchus shows exquisite epithelial metaplasia. It is surrounded by a thick wall of vascular, in places, hemorrhagic granulation tissue, and there is active organization of the exudate in the neighboring alveoli.

(c) The section shows the same lesions as described above, but confined to the bronchi and peribronchial tissue. There is no generalized edema as in block (a). The dilatation of the pus-filled bronchi is very distinct. (d) There is a suppurative and necrotizing bronchitis, and an organizing peribronchial exudate as described in (a) and (b). In another portion of the slide the bronchioles are lined with intact ciliated epithelium, but there are local thickenings composed of vascular granulation tissue. There is also marked perivascular fibrosis. (e) The section shows an additional feature of interest, namely, several areas of gangrene, in which there is complete loss of nuclear staining, and all structures are involved. Another striking feature is an area in which the alveolar walls are greatly thickened by the accumulation of numberless lymphoid and plasma cells in the spaces between the alveolar epithelium and the capillary wall. In some there is extensive organizing pneumonia, the plugs being well vascularized. *Skin*: Two blocks, showing a thin epidermis composed of only two or three rows of cells, covered by a relatively thick loose keratin layer. The basal row of cells shows an excessive melanin production. There are many chromatophores in the superficial corium, and some granules of extracellular pigment. The subepithelial portion of the corium shows a hyaline edema. There is no inflammation. The capillaries are collapsed and empty. The sweat glands and hair follicles show no lesions.

NOTE.—The case illustrates admirably the late effects of severe mustard-gas lesions of the respiratory tract. The injury was quite certainly incurred on August 7 or 8, so that the duration of life after gassing may be taken as 53 days. While the records of the Chemical Warfare Service show that the organization to which A. K. belonged was exposed to indiscriminate shelling on those days with yellow, blue, and green cross shells, it is probable that mustard gas was the principal agent concerned.

The skin lesions illustrate the persistent pigmentation. The lesions of the trachea were evidently very severe, the destruction even involving some of the mucous glands. There was little epithelial regeneration; what epithelium there was showed the customary metaplasia. There was a widespread suppurative and necrotizing bronchitis, which led to marked cicatricial thickening of the bronchi. In places there were abscesslike bronchiectases. The parenchyma about the bronchi showed an organizing pneumonia, but in some blocks there was an interesting chronic edema, with epithelial exfoliation and proliferation, and interstitial changes—lymphoid and plasma cell accumulation—in the alveolar septa. The picture in these regions resembles in many respects the pneumonia alba of congenital syphilis. Worth noting are the areas of gangrene.

CASE 103.—A. M., 2187370, Pvt., Co. F, 340th Inf. Died, on December 20, 1918, at 1.20 p. m., at Base Hospital No. 87. Autopsy No. 47, performed one and one-half hours after death, by Lieut. H. H. Robinson, M. C.

Clinical data.—October 23, gassed with mustard gas. No further details recorded. October 25, admitted to Base Hospital No. 87. On November 7, two weeks after gassing (?), developed bronchopneumonia, which never entirely cleared up. Illness marked by profuse mucopurulent expectoration. Died in collapse on December 20, a few minutes after aspiration of the chest.

Summary of gross lesions.—There is brown pigmentation of skin of knees and thighs and of scrotum. Both pleural cavities show firm adhesions. The lungs are voluminous and pink. Scattered through all lobes are numerous areas of grayish consolidation. In the left lung, in both lobes, there are numerous smooth cavities, varying from a pea to a walnut in size. Circulatory organs: Normal.

Additional note, dictated from preserved Army Medical Museum specimen of left lung: "Upper lobe: The pleura over a localized area in lower portion of the lobe is thickened with organizing fibrinous exudate; elsewhere smooth. Over the lower lobe there are a few delicate fibrous tabs. On section, the lung is generally dry and air-containing. About the bronchi and vessels, however, there are firm, yellowish-white zones of consolidation, becoming

more translucent at the periphery. About these again, there are irregular patches darker in color, which appear to be areas of organizing pneumonia. Beneath the thickened pleural patch in the upper lobe there is a group of large bronchiectasis with smooth walls. These are surrounded by opaque, grayish-yellow patches. The larger bronchi are lined with smooth, pale mucosa which in places has a scarred appearance."

Microscopic examination—Lung: A block taken through wall of the bronchiectasis shows that the cavity is bounded by granulation tissue, remarkable because of the great number of large foamy (lipoid containing?) cells included in it. Adherent or lying loosely upon the surface of the granulation tissue are many large multinucleated giant cells. Whether these have arisen from remains of the epithelium or are of the nature of foreign body giant



FIG. 38.—Case 103. Mustard-gas burn, 58 days' duration. Lung. Low-power drawing through bronchiectatic cavity. Peribronchial and periarterial fibrosis

cells can not be made out. The lung tissue about the cavities is collapsed and shows the usual interstitial fibrosis, with occasional alveoli lined by cylindrical cells. (Fig. 38.) There is much epithelial desquamation, and fibrous thickening of the septa in the better aerated regions. Some of the air spaces contain organized vascular plugs. Another section was taken through a patch of organizing pneumonia. There is histologically an exquisite interstitial and organizing process. (See fig. 21.) Especially interesting are the changes in the apparently regenerated epithelium. The band of hyaline necrosis, so frequently found lining ductus alveolares and alveoli in the acute cases, as well as in the primary influenzal pneumonias, is still very distinctly to be recognized; it is, however, condensed, hyaline, and stains very intensely with eosin. In many places it is being invaded and replaced with connective tissue, the nuclei of the cells tending to range themselves parallel to the wall of the

air space. The bronchioli in this section are for the most part lined with ciliated epithelium, but this is thrown up into corrugated folds, and many of the small bronchi are collapsed, and their lumen reduced to a narrow cleft. Acute inflammatory changes are still present in places.

NOTE.—A case of mustard-gas poisoning in which death occurred on the 58th day after exposure. The interpretation of the case is complicated by the fact that pneumonia, according to the brief clinical note, did not develop until two weeks after the gassing; there is no reference to previous respiratory symptoms. It is conceivable, therefore, that the interesting residual lesions in the lungs—interstitial and organizing peribronchial pneumonia, bronchiectasis, etc.—may have resulted from a primary influenzal pneumonia rather than from the direct gas injury. It is unfortunate that there is neither a description of nor material from the trachea available.

CASE 104.—M. L. A., Number —, Pvt., Co. L, 101st Inf. Died, June 11, 1918, at 11.15 p. m., at Base Hospital No. 18. Autopsy, 10 hours after death, by Lieut. B. S. Kline, M. C.

Clinical data.—March 31, gassed with phosgene at 2 a. m. Following this, shortness of breath and headache with vomiting. June 2, admitted to Base Hospital No. 18. Patient conscious, but stuporous and cyanotic. June 3, oxygen therapy begun and he was bled 325 c. c. The heart sounds at this time were clear and regular; tubular breathing was present over a small area at the left base. On June 4 and 5, his general condition seemed to improve. On the 6th, however, diffuse areas of consolidation were made out over the left lower chest. He also developed diarrhea on this day. June 8, patient was definitely weaker and very dull. Pulse full and fast. June 10, Cheyne-Stokes respiration, with long pauses. Pulse irregular and weaker. June 11, small area of consolidation in the right lung. Patient very restless, rapidly became weaker. Venesection, 600 c. c. Died at 11.15 p. m. Temperature, from admission on June 2 to his death, was never below 100.2°. Maximum, 104.8°, on afternoon of June 4. Pulse, 100 to 128. Respirations, 28 to 44.

Anatomical diagnosis.—Acute pharyngitis, esophagitis, laryngitis, and bronchitis, following phosgene (?) inhalation; extensive bronchopneumonia, involving all lobes; acute lymphadenitis of regional lymph nodes; acute colitis; pulmonary edema, terminal; cardiac dilatation, more marked on the right side.

External appearance.—No cutaneous lesions. Skin has a muddy color, but there is no pigmentation recorded. Conjunctivæ and other mucous membranes pale. Slight clubbing of fingers and toes.

Gross findings.—*Pleural cavities:* Fibrous adhesions are found over the lateral and posterior surfaces of all lobes, especially the middle and lower on the right side. In the left pleural cavity are a few cubic centimeters of clear fluid, and a few adhesions binding the under surface of the lobe to the diaphragm. *Right lung:* Weighs 840 grams. *Left lung,* 1,020 grams. All lobes are voluminous, cushiony, soggy, and solid. The pleura is thickened in the regions showing the fibrous adhesions mentioned above; elsewhere it is thin and delicate. The glands at the hilum considerably enlarged, pulpy, edematous and injected. The bronchi show marked diffuse injection, with suggestion of ulceration of the epithelium. In the lumina there is blood-tinged thin viscid fluid. On section of all lobes a dull gray red surface presents mottled with pinhead to grape-seed sized dull reddish-yellow areas. The surface is moist, and on pressure, a considerable amount of thin blood-tinged fluid exudes. When this is wiped off on the knife, a considerable portion of each lobe shows a dull, slightly granular, reddish-gray consolidation, which at first suggests a lobar type, but on close inspection, relatively few alveoli here and there are found to be involved. Although the tissue floats in water, the pseudo-lobar consolidation is very extensive and the tissue is friable. In the finer bronchioles, the exudate is perhaps slightly more viscid than in the larger branches. The two types of consolidation are more marked on the left side, and particularly in the left lower lobe, where some of the smaller areas are firm and look quite like miliary tubercles. In the other lobes, some of the smaller solid areas have a similar appearance. There is little hemorrhage anywhere. The blood vessels contain large currant-jelly clots. *Organs of neck:* *Larynx and trachea* show moderate diffuse injection of the mucosa, with adherent fibrino-purulent exudate here and there in small amount, especially in the region of the true vocal

cords. The process continues over the brim and involves the upper portion of the esophagus, pharynx, and base of the tongue. The tracheal and cervical lymph nodes are moderately to considerably enlarged, injected, pulpy. *Tonsils*: Small and scarred. *Heart*: Weighs 360 grams; right auricle and ventricle moderately dilated and the tricuspid and pulmonary rings considerably stretched. Myocardium of left ventricle pale, moist, and greasy. *Gastrointestinal tract*: Stomach normal. In the cecum there is patchy injection of mucosa, and in the transverse and descending colon there is, in addition to the injection, a small amount of adherent exudate on the surface of the mucosa. The mesenteric glands are slightly enlarged, soft, and pale. Remaining viscera show no significant changes.

Microscopic examination: Pharynx or upper esophagus: The mucosa is continuous except over a small area where there is superficial ulceration, with a little adherent exudate and localized edema and inflammatory infiltration. *Trachea*: No section. *Lung*: (a) Bronchi are lined with multiple layers of epithelial cells, the superficial layer of which is composed of flattened nonciliated cells. The mucosa is thrown into rugæ, there being a granular coagulum beneath it. The lumen contains blood and granular material, with very few leucocytes. Throughout the parenchyma the alveoli are filled with red blood cells, granular coagulum, and only here and there are denser collections of leucocytes, polymorphonuclears, and mononuclears. In some air spaces are numerous foamy exfoliated epithelial cells. The most striking feature is the almost universal regeneration of alveolar epithelium; in places the proliferating cells form solid nests or sprouts almost completely filling the air spaces. Individual hypertrophic cells are found, and mitoses are fairly numerous. The septa are edematous, contain more than the normal number of leucocytes, chiefly large and small mononuclears. There are stout fibrin threads in the capillaries. A small artery in the section contains a well-formed recent thrombus. (b) There is a somewhat more acute process, with purulent bronchiolitis and inflammation of the ductus alveolares, and hemorrhagic edema in the surrounding lung. Epithelial regeneration is less marked than in the previously described section. (c) In addition to the features above described, there is a striking hyaline necrosis of the alveolar walls. Where the epithelium is being regenerated, it is often separated from the alveolar capillary by edematous tissue in which are proliferating fibroblasts and large and small mononuclear cells. No bacteria are found in Gram-stained sections. *Liver, spleen, myocardium, adrenals, and kidneys* show no lesions of special interest.

Bacteriological examination.—Smears made of the exudate from the larynx show numerous lanceolate diplococci, Gram-positive; also numerous biscuit and rounded cocci in groups. Gram-positive and a moderate number of intracellular and extracellular Gram-negative bacilli of small size. Smear from the bronchus shows moderate numbers of intracellular Gram-positive and negative cocci and diplococci, and groups of small Gram-negative bacilli. Smear from a small consolidated area shows numerous intracellular Gram-negative bacilli. Smear from the large consolidated area shows a small number of Gram-positive diplococci and a few groups of Gram-negative small bacilli. Cultures from the larynx shows innumerable staphylococci. Cultures from bronchus: Staphylococci and Gram-negative bacilli, tiny and of good size. Culture from small consolidated area shows predominating organism a staphylococcus. From the large consolidated area, minute Gram-negative bacilli and a few staphylococcus colonies.

NOTE.—Aside from the superficial erosions of the pharynx and larynx, there is nothing to suggest that the lesions are due to the toxic effect of gas, either mustard or, still less, to a suffocative gas such as phosgene. The history does not state whether symptoms persisted after gassing until admission to Base Hospital No. 18, two months later, nor are additional data as to the character of the gas available. The pulmonary lesions are those of influenzal pneumonia as seen in the fall and winter pandemic, and would coincide with an onset about June 2. Whether a previous gassing determined the severity of the pulmonary lesions at a time when the prevailing type of the disease was mild and rarely followed by pneumonia, remains uncertain.

CASE 105.—W. K., 2566932, Corpl., Co. A, 107th Engineers. Died, October 21, 1918, at 3 a. m., at A. R. C. M. Hospital No. 5. Autopsy No. 92, performed six hours after death, by Lieut. H. W. Hundling, M. C.

Clinical data.—On August 5, patient was exposed to shelling with yellow, blue, and green cross shells, while his detachment was advancing through valleys in rolling country (sector of 64th Brigade). On August 12, there was bleeding from the nose and lungs. September 15, admitted to A. R. C. M. H. No. 5. September 19, pulse bad. Chest full of râles; profuse expectoration; sputum negative for tubercle bacilli; streptococci and pneumococci in cultures. Daily temperature of 101°, respirations 24, pulse 104. Marked emaciation.

Summary of gross lesions.—No external lesions. Marked emaciation. Pleural cavities show friable adhesions. Lungs firm posteriorly, crepitant anteriorly. Cut surface moist; scattered through all lobes are areas of peribronchial thickening, coalescing to form broad areas of consolidation. Circulatory organs normal. *Organs of neck.* (Note dictated from preserved Army Medical Museum specimen). The specimen consists of *tongue, trachea, and larynx* preserved in formalin. The tongue and pharynx show no changes. The inferior surface of the epiglottis shows a large depressed brown patch, which is present also along the tracheal surface of the cords. It is not clear whether this may not be an artefact due to drying. The upper part of the larynx shows a thin, smooth lining, with irregular pearly scarred areas. Further down, the tracheal wall becomes rough, sandy and congested, and covered here and there with little flakes of necrotic exudate. Along the right border, about 2 cm. above the bifurcation, are two punched-out ulcers which extend through the eroded cartilages. They are from 2 to 3 mm. in diameter.

Microscopic examination.—Blocks were taken from preserved Army Medical Museum specimen. *Epiglottis:* The cartilage is covered on both sides by dense layered squamous epithelium, like that of the pharynx or esophagus. There is no pigmentation, and the brown color noted in the specimen was probably due to drying. The subepithelial tissue contains dense collections of lymphoid cells, but there are no other evidences of inflammation. The glands are normal. *Trachea:* Section taken at level of thyroid. Here too the epithelium is squamous and devoid of cilia. It is quite thin, consisting of only three or four rows of cells. There is no keratinization of the superficial cells. The subepithelial tissue is very dense and scarlike, and contains few blood vessels. Some of the glands are normal, others are atrophic, still others are distended with secretion. The glands are entirely missing over large areas. Section taken through small ulcers shows the following: At the margin, the epithelium is thickened and squamous. The ulcer is quite sharply defined, and extends down to the cartilage, and even undermines it. The base is composed of dense scar tissue infiltrated with lymphoid cells. *Large bronchus:* Completely filled with a fibrinopurulent plug. The lining consists of loose granulation tissue. There is much edema, hemorrhage, and inflammatory infiltration of the bronchial wall.

Bacteriological examination.—*B. influenzae* in culture from lung after death.

NOTE.—After 77 days, marked changes were found in the trachea. The epithelium was converted permanently into a dense stratified layer composed exclusively of squamous cells, which, however, had not become keratinized. The subepithelial tissue was dense and scarred, the mucous glands atrophic or wholly lost, and the smooth muscle fibers had disappeared. There were also several deep localized ulcers in the lower portion of the trachea. In the large bronchus taken for examination, there was no regeneration of the epithelium, and the lining granulation tissue lay exposed.

It is probable that these lesions of the upper respiratory tract are the late results of exposure to mustard gas, although there is no reference to cutaneous burns in the history, and the records of the Chemical Warfare Service show that the patient had been subjected to shelling with mixed types of gas.

CASE 106.—C. M., No.—, organization (?), rank (?). Died, December 8, 1918, at U. S. A. General Hospital No. 19, Oteen, N. C. Autopsy by (?).

Clinical data.—The following is a verbatim transcript of the history which accompanied the preserved museum specimen. No further information in regard to the case is available. "Enlisted September 10, 1917. June 20, 1918, to trenches. June 24, hit with mustard gas and blinded for four days. He had black spots all over and could not see well for six weeks. Throat quite sore. Has been in hospital ever since. Pleurisy, August 15.

Walked into U. S. A. General Hospital No. 19, Oteen, N. C. with slight cough and expectoration, dyspnea, and occasional pains in left lumbar region. Looked well. Right side, dullness above third rib, and practically throughout posteriorly. Moist râles from fifth rib and sixth dorsal spine down. Left side, markedly diminished expansion; dullness above fourth rib from eighth dorsal spine up. Moist subcrepitant râles ninth to fourth dorsal spine. Slight pretibial edema. Cardiac fibrillation and pulse deficit. Fluoroscopy, apices cloudy and do not clear on coughing. Right hilus shows very dense shadow to diaphragm. Tuberculosis, pulmonary, chronic, oldest and most extensive in upper left lobe. Abnormal densities at both bases.

"Autopsy.—Fairly well nourished. Pink adhesions which completely obliterate right pleural cavity. Dilatation of right heart, slight. Liver, hypertrophied, 12 cm. below costal margin in midline. Pleural adhesions on left at base and posteriorly. Greenish pus in trachea. No gross changes in kidneys. In small bowel are a number of dark areas several feet in length, and slight ulcerations are noticed in several parts. In the neighborhood of the cecum these areas are more marked. Appendix slightly inflamed. Urinary bladder, slightly ulcerated on the superior surface."

The following additional note was dictated upon receipt of the Army Medical Museum specimen:

The specimen consists of formalin fixed slabs of the *right lung* passing through the three lobes. The pleura is covered with tabs of fibrous adhesions. The upper lobe, in its posterior two-thirds, is of translucent texture, very slightly air-containing; only here and there a few well-aerated patches. Near the hilum there is a cross section of a bronchus 3 mm. in diameter, completely filled with a fibrinous plug. This is surrounded by opaque creamy white airless tissue from which radiate fibrous strands to join the small interlobular septa. The section passes also through a number of smaller bronchi plugged with exudate, and with thickened walls composed of dense opaque white tissue. Lower lobe: A large portion consists of very firm white or yellowish-white opaque tissue, absolutely airless, in which bronchi and blood vessels seem to be largely obliterated. Between these patches, the architecture of the lung is still recognizable, but the alveolar walls are thick and the air content much diminished. The smaller and larger bronchi are extremely thick-walled. The lumina are narrowed and their mucosa appears rough and eroded. Near the posterior border, there is an irregular, but smooth-walled cavity, the lining of which is blood stained. The communication of this with a bronchus can not be demonstrated because of the thinness of the specimen. The middle lobe shows only moderate bronchial thickening and is air-containing. A group of lymph glands at the hilum appears to be completely caseated, although they are firmer than ordinary tuberculous glands. In no portion of the lung are there seen definite tubercles, although the gross resemblance of certain areas to diffuse tuberculous caseation is very close. (Fig. 39.)

Microscopic examination.—*Lung:* (a) The block is taken through the area of gelatinous edema at the base of the upper lobe, and includes the edematous interlobar septum. (Fig. 40.) The alveoli are wide and almost without exception, distended with a homogeneous coagulum, in which are scattered large rounded alveolar cells containing black pigment. The alveolar septa are compressed and there is very little blood in the capillaries. Such attached alveolar cells as can be recognized seem hydropic and project into the alveolus. There are many cells with pale distorted nuclei, probably fibroblasts. The section includes two small bronchi. The larger of these has an irregular slit-like lumen like that of an intracanalicular fibroma, which is filled with pus. The epithelium is beautifully ciliated, showing no metaplasia. The wall is tremendously thickened by a rather dense and not very vascular granulation tissue in which are numerous lymphoid and plasma cells. These cellular infiltrations extend into the adjacent alveolar septa. The interlobar septum is edematous forming a broad pink-staining band. Under the high power, a delicate thready reticulum can be distinguished. From the margin, there is an ingrowth of delicate blood vessels with pale swollen endothelium. Scattered through the edematous zone, there are groups or little colonies of large rounded cells with very pale nuclei, which are identical with the proliferating pleural mesothelium, and are probably derived from it, having migrated into the plasma clot after the fashion of a tissue culture. Here and there these cells are multinucleated. There are also scattered small lymphoid cells, but very few fibroblasts and it



FIG. 39.—Case 106. Mustard-gas burn, 5½ months' duration. Lung, showing marked peribronchial and perivascular fibrosis, interstitial fibrosis, organizing pneumonia chronic edema, bronchiectasis

can not be said that the edematous tissue is becoming organized. (b) The block is taken from the anterior and lower portion of the upper lobe, passing through the bronchus described in the gross. (Fig. 41.) The exudate which fills the lumen with a complete plug is composed chiefly of polymorphonuclears, well preserved at the periphery, fragmented at the center. The bronchus is lined by a very thick wall of granulation tissue, the epithelium having been quite destroyed. This granulation tissue is remarkable because of the very dense plasma cell infiltration. In many fields, the plasma cells completely fill the interstices

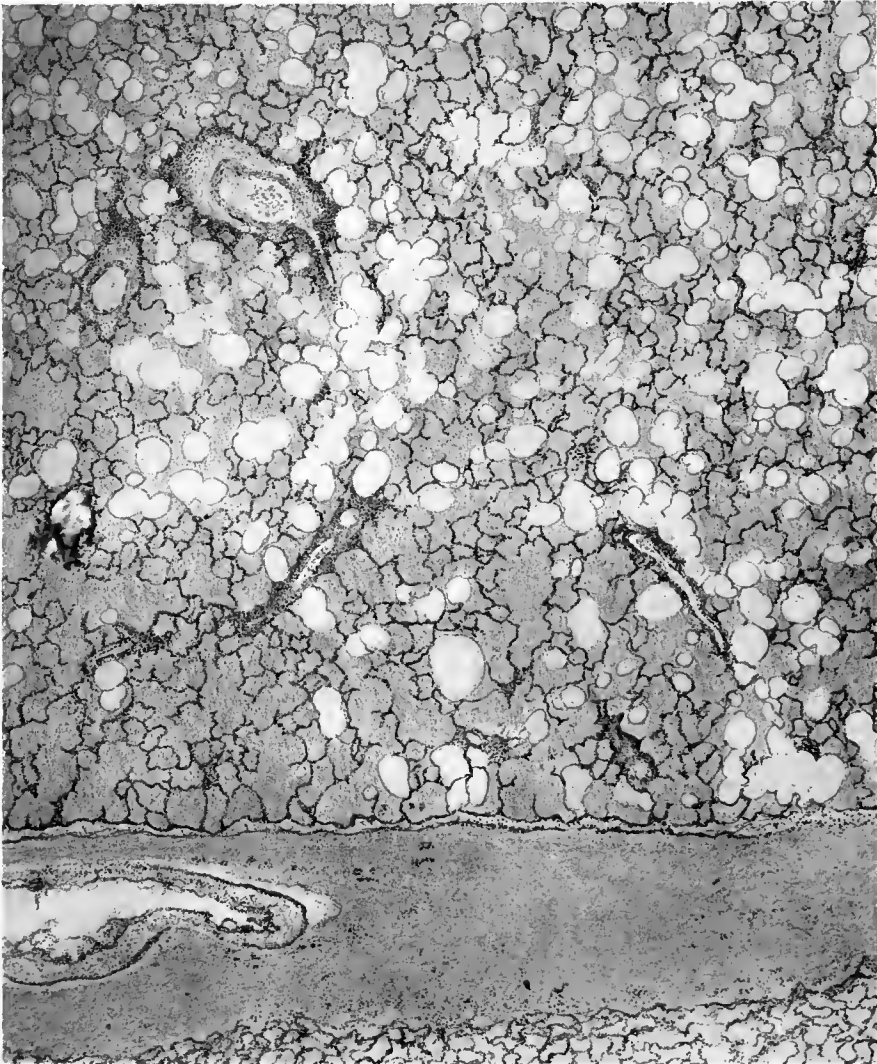


FIG. 40.—Case 106. Lung. Section (a) Edema of alveoli and interlobular septum

between the sprouting capillaries. Further out, the granulation takes on rather the character of scar tissue, and extends in the form of radiating strands into the neighboring parenchyma. Here the alveoli are widely separated, and their lumina irregularly distorted. They are lined with columnar epithelium, and contain exfoliated cells. Often the wall of the alveolus is thrown up in papillary folds. Although the bronchus is fully 5 or 6 mm. in diameter, there are no remains of cartilage, muscular wall or mucous glands, all of these structures having apparently been replaced by granulation and scar tissue. Between the fibrous

strands radiating from the bronchus, the alveoli are very large, and filled with edematous coagulum and exfoliated epithelial cells. The septa are infiltrated with lymphoid and plasma cells. Smaller bronchi in the section are lined with intact epithelium, but they appear collapsed into irregular slits. The small pulmonary arteries are surrounded by broad bands of scar tissue, from which, also, strands extend into the neighboring parenchyma. (c) The block is taken from the opaque whitish tissue in the anterior portion of the lower lobe, which grossly resembled tuberculous caseation. Microscopically, the tissue proves to be a rather avascular granulation tissue which, over large areas, has completely obliterated the normal lung structure. There is a remarkably dense plasma cell infiltration, these comprising practically the only type of wandering cell in many fields. In areas where the alveolar

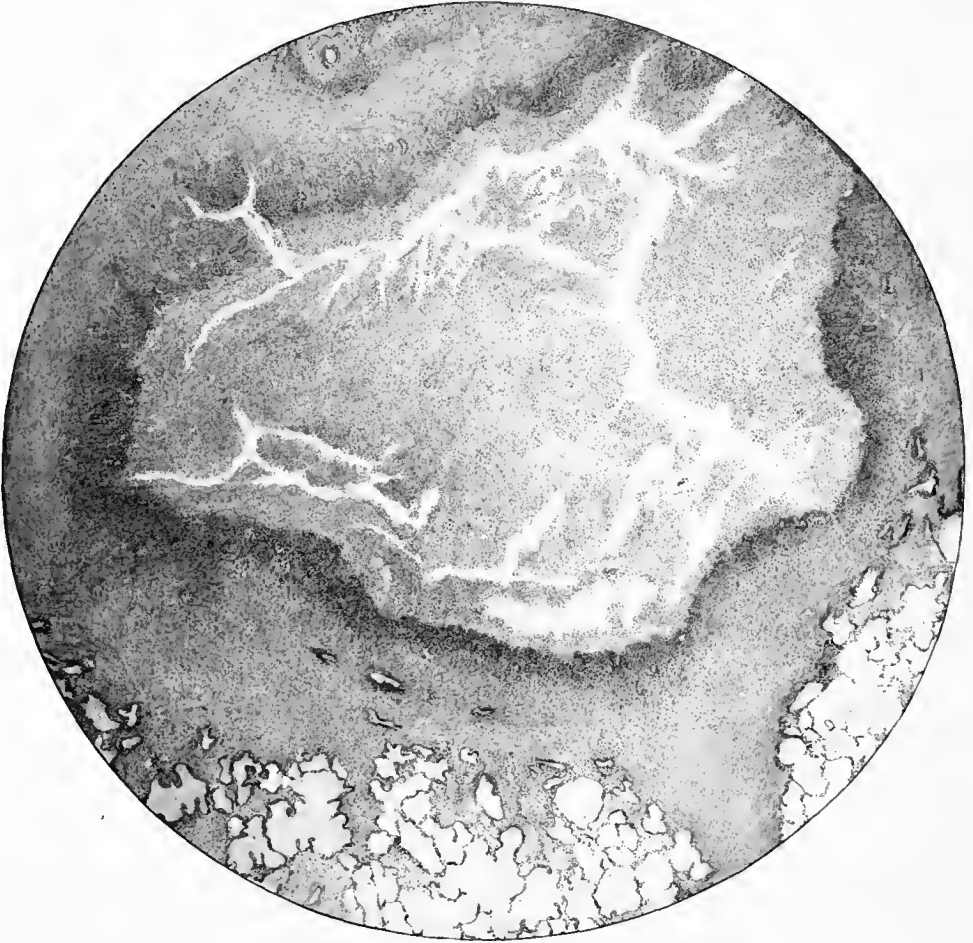


FIG. 41.—Case 106. Lung. Section (b) through cavity in the upper lobe

structure is still discernible, the septa are thickened and infiltrated. As in the other section, the arteries are surrounded by broad bands of connective tissue, and there is marked interlobular fibrosis. (Fig. 42.) (d) Block taken through a group of greatly thickened bronchi, surrounded by scar tissue, near the hilum of the lower lobe. The lumina are narrowed and their wall thrown up into corrugations. The epithelium is high, stratified and beautifully ciliated, showing no squamous cell metaplasia. The walls of the bronchi are enormously thickened by dense scar tissue, thickly infiltrated with plasma cells. (Fig. 43.) The mucous glands are preserved, and are in hypersecretion. The cartilages likewise are still present and show no degeneration. The surrounding pulmonary tissue shows the same changes

that have been described in previous section. A large branch of a pulmonary artery presents interesting lesions. There is marked intimal thickening by a loose edematous (fatty?) fibrous tissue, with corresponding thinning of the muscular coats. The adventitia of this and of all the smaller arterial branches is tremendously thickened. (c) Block taken through the wall of the supposed bronchiectatic cavity in the posterior portion of the lower lobe. Microscopically, there is no certain evidence that this cavity is a bronchiectasis, since there are no remains of the normal bronchial structures. The wall is formed simply by the irregularly thickened septa of the adjacent lung tissue, the rounded walls projecting freely into the cavity, which therefore has neither a continuous epithelial lining, nor one composed of

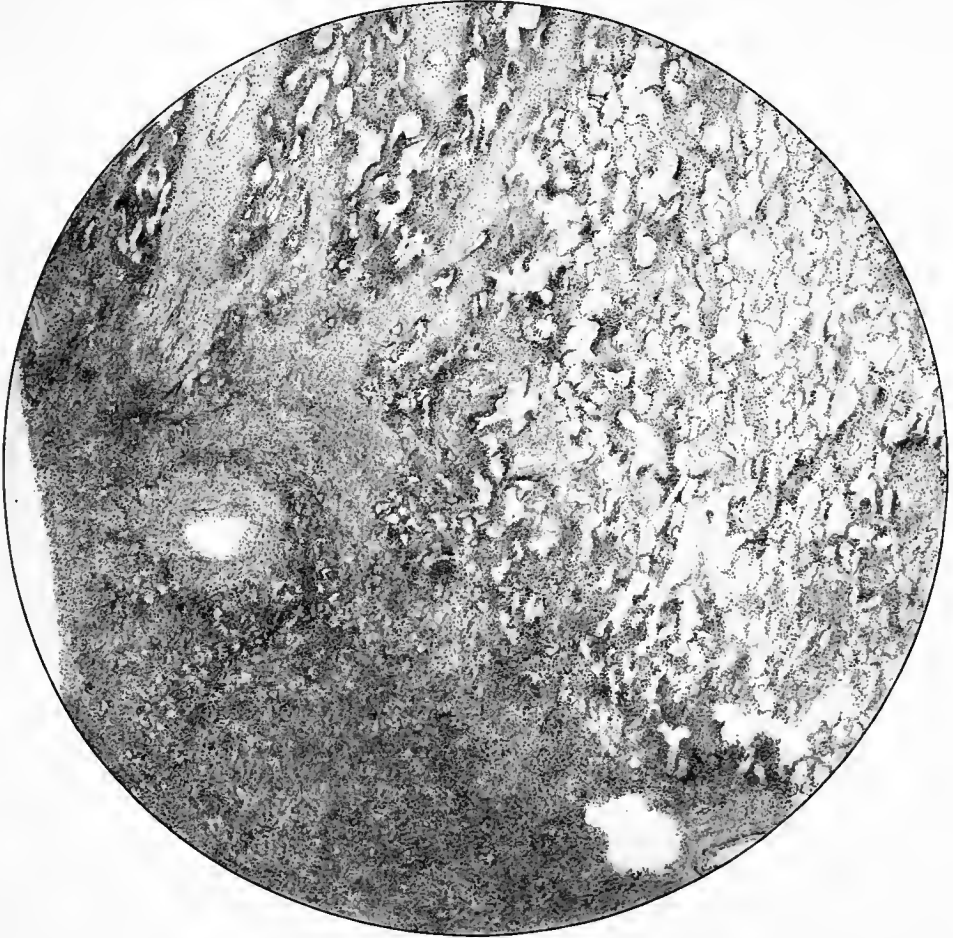


FIG. 42.—Case 106. Lung. Section (c) taken from opaque whitish tissue in anterior portion of lower lobe. Lung structure over large areas obliterated by poorly vascularized granulation tissue, densely infiltrated with plasma cells

granulation tissue. The cavity appears to be simply a defect in the lung substance, in an area which shows an extreme interstitial fibrosis of the type described. The exact way in which this cavity has been formed is not clear. In only one portion is there a definite lining of granulation tissue with tangential compression of the neighboring alveoli. (f) A section taken from the upper lobe, in an area of relatively normal lung tissue, in which, however, there were a few thickened bronchi and blood vessels. Microscopically, the lesions resemble those in block (a), save that there is less alveolar edema. The only new feature is a rather marked emphysema. Worth noting also are the lymphoid follicles with definite germinal centers, which are seen in the scar tissue about the bronchi. *Primary bronchus:* The

epithelial lining is intact over most of the circumference, and is composed of several layers of cells, the superficial row normally ciliated. The section, however, passes through a small patch of squamous epithelium, continuous on either side with the ciliated epithelium, but somewhat thicker. In this area there are numerous mitotic figures. There is persistent metaplasia in some of the ducts of the mucous glands, while others are invested with normal cylindrical epithelium. The submucosa is thick and dense, and filled with lymphoid and plasma cells in great numbers. The acute inflammatory process has disappeared, and polymorphonuclears are found only on the surface, or between epithelial cells. The mucous glands are in active secretion, and in no wise abnormal. The cartilages also are unchanged.



FIG. 43.—Case 106. Lung. Section (d), through thickened bronchi at hilum of lower lobe

The adjoining lung tissue appears compressed. *Secondary bronchus:* In places denuded of epithelium, the wall being formed by a dense cellular and not very vascular granulation tissue. Where epithelium is present, it is for the most part quite normal in structure, the cilia being very distinct. Here and there, and especially about the openings of the mucous ducts, the epithelial cells are heaped up irregularly and the superficial cells are not differentiated. That the denuded areas are really ulcerated, and not merely exposed by the post-mortal exfoliation of cells, is indicated by dense plasma cell infiltration. *Bronchial lymph node:* The changes are surprisingly slight, although the gland as a whole appears hyperplastic, and is strikingly free from pigment. There is much periglandular fibrosis, and a branch of the pulmonary artery included in the section shows a marked intimal fibrosis.

NOTE.—The case is one of particular interest. Death occurred 167 days, or approximately five and one-half months, after gassing with mustard-gas. The respiratory lesions found at autopsy may be regarded without qualification as the late results of this injury. Clinically, the patient presented pulmonary symptoms and physical signs closely simulating those of chronic pulmonary tuberculosis, and this diagnosis was made during life on the basis of the fluoroscopic findings, although there is no record of tubercle bacilli having been found in the sputum.

CASE 107.—F. S., Pvt., Co. A., 126th M. G. Bat. Died, May 16, 1919, at base hospital, Camp Lee, Va. Autopsy No. 49, eight hours after death, by Lieut. Charles H. Manlove, M. C.

Clinical data.—Patient was gassed October 14, 1918, on the Toul sector, with mustard gas. He was not burned much on the skin, but was rendered unconscious for a short time. Taken to the field hospital and from there transferred to Base Hospital No. 45, then to Base No. 210, and then to Base No. 87. Later sent to Camp Lee, where he arrived about April 6, 1919. At the time of the gas attack, the gas mask was rendered useless as the can was broken from the contact. As gas entered the mask, he began to vomit and then the mask came off entirely, and he inhaled the pure gas. The patient was very much emaciated, cyanotic, and markedly dyspneic. His breathing was better at night, allowing him to sleep very well. He coughed continuously and expectorated considerably. Had sense of constriction in the larynx. Physical examination of the chest showed harsh breath sounds, showers of moist râles, vocal fremitus decreased over left base. Heart rate was regular.

Anatomical diagnosis.—Stricture of trachea, following gas injury. Tracheotomy. Chronic tracheitis. Subcutaneous emphysema. Chronic bronchitis. Passive congestion of viscera

External appearance.—Well developed, poorly nourished. No ocular or cutaneous lesions. Subcutaneous tissue of the entire neck and upper third of sternum are emphysematous. In the midline of the neck, over the thyroid there is a recent operative wound, measuring about 3.5 cm. in length, with a central opening, which extends into the trachea, from which a mucopurulent material exudes.

Gross findings.—*Trachea:* Vocal cords and mucous membrane above the trachea normal. Mucous membrane just below the vocal cords show marked thickening, which extends to the bifurcation of the trachea, the lumen throughout being markedly diminished in diameter. This is especially evident over an area of 3 to 4 cm. in length, beginning about 3 cm. below the stricture. Mucous membranes of trachea and bronchi are reddened and coated with a thick mucopurulent material. *Lungs:* Are rather large, and crepitate throughout, and crackling is present in some places. The pleura covering the lungs is spotted with black pigment over its entire surface, giving the surface a blackish gray appearance. After preservation in Kaiserling, section shows lung tissue to have been air containing throughout. Bronchi contain plugs of mucopurulent material. Apices appear slightly more compact than the remaining portion of lungs. *Heart* and the remaining viscera are normal. (Fig. 44.)

Microscopic examination.—Block 1. *Trachea:* The section is taken longitudinally through the scarred stenotic tissue below the thyroid. There is a thin layer of stratified nonciliated epithelium in places, but the greater part of the submucosa lies exposed. It is converted into dense scar tissue, 2 to 3 mm. in width. In the depths are groups of mucous glands and ducts, some dilated, other atrophic, and surrounded by lymphoid and plasma cells. There is intracellular hemosiderin in the more superficial portion of the tissue. The cartilages are intact. *Secondary bronchus:* Block 2. The epithelium is partially exfoliated, but normally ciliated, where still preserved. There is congestion of the bronchial wall, but little or no inflammatory change or scarring. The mucous glands are numerous and in active secretion. *Lung:* Block 3. Some of the alveoli are collapsed, others filled with edema fluid, still others emphysematous. There is excessive deposit of anthracotic pigment with small areas of fibrosis where the pigment is most abundant. The septa are a little thickened, and there is definite fibrosis of the perivascular connective tissue and of the interlobular septa. The small bronchioles are filled with columnar ciliated epithelium and contain no exudate. Many are corrugated and appear contracted or collapsed, others are slightly dilated. Block 4. Emphysema and anthracosis. Block 5. Somewhat more congested. No other significant changes.

Bacteriological examination.—Cultures from bronchial contents show staphylococcus.

NOTE.—Death six months after exposure to concentrated mustard-gas. This resulted in little permanent damage to the lower respiratory passages,

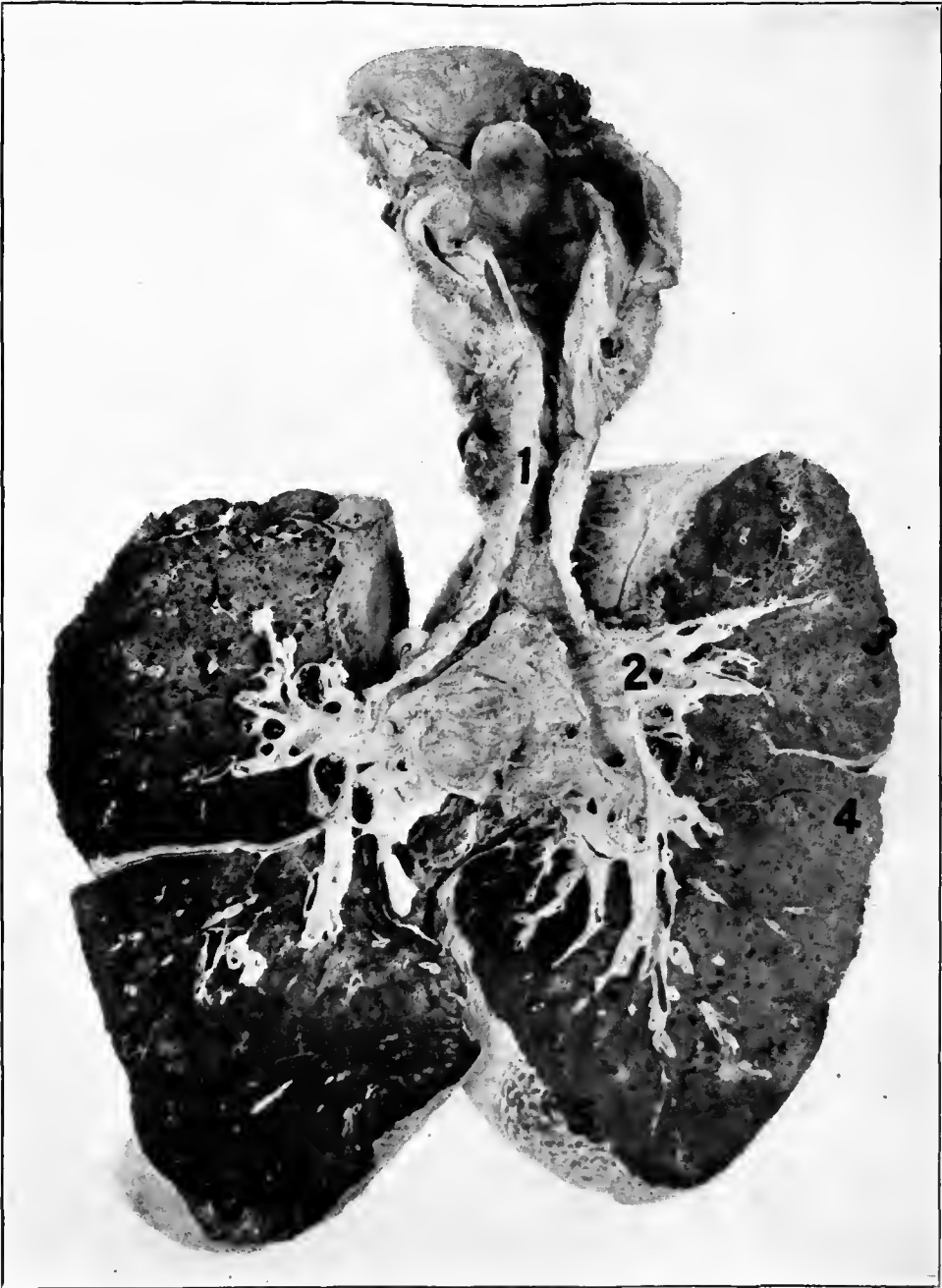


FIGURE 44.—Case 107. Late stricture of trachea showing mustard-gas inhalation

but produced a marked cicatricial stenosis of the trachea requiring tracheotomy. Epithelium still present in these scarred areas is of the squamous non-ciliated type.

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CHAPTER VII

SYMPTOMS AND TREATMENT

Here will be found a textbook description largely compiled from information furnished by our Allies when we entered the war, and later. They were also the source of the various circulars of instruction which emanated from the offices of the chief surgeon and the Chemical Warfare Service. The most important of these circulars are printed elsewhere in this volume. This chapter then contains little original with us and is justified only by the fact that the majority of our readers will not have easy access to the authorities responsible for first making of clinical record observations relating to the symptoms and treatment of the various poisonous gases employed during the war.

In the discussion of the symptoms which followed exposure to toxic gases, the classification of these agents according to their physiological action, as given in Chapter III, is employed. The symptoms of carbon monoxide poisoning are also considered, since this gas, though not a combat gas, was responsible for some casualties.

It should be remembered that the character of the symptoms due to any of the combat gases was materially dependent upon the concentration of the gas to which the individual was exposed, whether high, medium, or low, and the period of time during which he was subjected to its action. Exposure to a low concentration for a prolonged period produced symptoms similar to those from exposure to a high or a medium concentration for a much shorter period.

While it has proved practical and convenient to group the various gases used during the World War, viz, lung irritants, vesicants, etc., this grouping is based on their most important action. That is to say, because, for example, a lung irritant is so classified this does not imply that its sole action is irritation of the lungs. On the contrary, all the toxic gasses employed exerted effects other than their group name implies.

SYMPTOMS

LUNG IRRITANTS

The chief gases classified as lung irritants were phosgene, diphosgene, chlorine, and chloropicrin. Nitrous fumes, while not used for combat purposes, are also included, as they gave rise to a similar train of symptoms, while dichlorethyl-sulphide (mustard gas) is classed with the vesicant group, it possesses lung irritant properties which call for consideration.

The chief characteristic of gases of this group is the irritation of and damage to the deeper respiratory passages, especially the alveoli of the lungs, which they produce, with resulting inflammatory exudation of fluid, acute pulmonary edema, and frequently death by asphyxia. In addition to their action as lung irritants, some of these gases are effective lacrymators.

While the presence in one patient of symptoms characteristic, not of one but of several gases, was at times confusing, it was usually possible for a medical officer to determine very promptly that intoxication with a gas of lung-irritant group had occurred. On the other hand, to determine which gas of this group was responsible for the symptoms was difficult. Fortunately, this was of little clinical importance.

GENERAL SYMPTOMS OF LUNG IRRITANTS

Certain differences in character and action of the individual gasses of this group will be noted later. The following detailed consideration of the general symptomatology of the group is based largely on the effects actually produced by phosgene and the similar chemical compound, diphosgene, since the majority of the casualties in American troops were due to these two substances.

The immediate effect of a lung-irritant gas in high concentration, aside from irritation of the eyes, was suffocation, due seemingly to spasmodic arrest of respiration, which, if the concentration of the gas was very high, often killed almost instantly by respiratory paralysis. These were the so-called fulminating intoxications. Usually, however, as the concentration of the gas was not commonly as high as this, the initial suffocative phase was passed over safely. Other effects from the gas were delayed. The victim even felt comparatively well during the ensuing intermission, though on examination his pulse and respiration usually were found accelerated and his temperature subnormal. Sometimes he complained of headache, substernal and epigastric pain, some irritation of the eyes, slight cough, and a sense of constriction in the chest. Nausea and vomiting were common. The latter effects appeared in from two to six hours. The predominant manifestation then was pulmonary edema. In very light cases only, the patients seemed to escape this edema and showed merely bronchitis. The pulmonary edema was general, or was localized in certain areas of the lungs. Its extent and the rapidity of its development seemed to depend on two factors, the amount of gas inhaled and the efficiency of the heart. The importance of the latter was emphasized by the ill effects due to increased strain incident to muscular exertion and by the disproportionately large number of cases with chronically disordered hearts and lungs that terminated fatally.

As the quantity of fluid which escaped into the alveoli of the lungs increased, symptoms appeared, caused by its presence. The chief were tachycardia, dyspnea, cyanosis, and cough, with the expectoration of frothy serous fluid. Dyspnea was an early sign and a danger signal. The cyanosis was usually accompanied by a peripheral venous engorgement, the so-called "blue" cases, but not infrequently, and especially in the more severe intoxications, the skin was pale and the peripheral veins collapsed, the so-called "gray" cases.

The clinical features of the two types of cases just mentioned were often distinctive. In the first ("blue") group, in which the patients showed definite venous engorgement, there was marked restlessness, the face was congested and deeply cyanosed, the lips and tongue were a full blue color, and frequently there was visible distention of the superficial veins of the face, neck, and chest. The respiration was increased in frequency and at times deeper than normal. Cough might be present and the expectoration of large quantities of thin, frothy, blood-tinged fluid was more common than in the "gray" cases. The pulse was full and strong and the rate about 100 per minute.

Cases in the "gray" group showed an ashen pallor rather than a deep cyanosis, the lips being pale and leaden colored. There was marked tachypnea and shallow respiration. Though the lungs were intensely edematous, there was often little expectoration, but cough was frequent. The pulse was weak and thready and the rate 130 to 140 per minute. The blood pressure was low. Marked collapse was present. Needless to say, the prognosis in this group was far worse than in the former.

In both, the edema first developed in the upper lobes of the lungs and extended downward. It was manifested by fine crepitant râles and relative dullness, but this was sometimes masked by superficial emphysema.

Digestive disturbances were common, notably nausea, vomiting, and anorexia. The spleen was often enlarged and icterus (seemingly a cardiac icterus resulting from passive congestion of the liver) sometimes was observed. Renal disturbances were not important. Albuminuria occasionally occurred, oliguria was common, but prolonged anuria was unusual. Moderate excitation, anxiety, and restlessness were frequently seen, offering a sharp contrast to men gassed with the fumes of dichlorethylsulphide (mustard gas). In some instances patients were semicomatose, with a muttering delirium, but, as a rule, they could be aroused to answer questions. Sometimes the respiration increased, even to 60 and 80 per minute, and was frequently labored and superficial. In many patients the pain became very severe and they moaned continuously. A thin, serous, foaming, blood-tinged expectoration was frequently present, especially after spasms of coughing. This fluid flowed from the mouth and nose until a mushroom-shaped collection of bloody froth formed on the face.

In cases progressing unfavorably, the respiration continued accelerated, the pulse grew more rapid and feeble, sonorous tracheal râles became audible, bloody froth exuded from the mouth, and death occurred. Usually this was in the second half of the first day, more exceptionally on the second or third day.

The danger period in all uncomplicated cases was usually passed by the end of 72 hours, and then followed improvement, with subsidence of the pulmonary edema. This stage was ushered in by the slowing of the pulse, which returned to normal and then fell below normal, to 60, 50, or even 40 beats per minute. The heart, however, remained irritable, and the slightest exertion increased the pulse rate to over 100, prolonged rest then being required to reduce it to normal. The arterial tension remained low for weeks.

As a rule, a patient recovered rapidly after the third day, and at the end of the week was fully convalescent. So rapid and complete might be the reabsorption of the fluid from the lungs that one who, in the acute stage, had showed the usual signs of extensive pulmonary edema, presented hardly any physical signs in the chest eight or nine days after exposure to the gas.

Complete recovery of cases of even moderate severity often required a very considerable time. Convalescent patients occasionally showed for some time a certain amount of digestive disturbance, associated with pain in the epigastrium, which was frequently accentuated after taking food, and loss of appetite. Bronchitis and pain in the chest occurred in a number of such patients, but yielded readily to treatment. Lassitude was common.

Certain patients continued to have precordial pain, dyspnea, exhaustion, and persistent tachycardia after exertion. After a brief period of moderate exercise they looked exhausted and obviously suffered from respiratory distress, while the pulse rate for several minutes remained higher than would have been the case with a normal person.

Other convalescent patients, and they were less common than those just described, had recurrent attacks of spasmodic dyspnea. These attacks might occur every night, or might be separated by an interval of a week: more than

one sometimes occurred during the same night. During the attack, which lasted from 5 to 30 minutes, the patient sat up in bed, his respiration was shallow and rapid, but not difficult, being very different from that shown in an ordinary asthmatic attack. Slight cyanosis might be present, but usually the color remained normal, and the patient appeared anxious rather than acutely ill. During the attack the pulse was usually slow and full, but might be rapid and almost impalpable.

In the great majority of these gas cases the symptoms ceased completely, and many patients who had been gravely ill were in time returned to full duty in the field. In a certain number of cases recurrent bronchitis and emphysema followed.

The precise cause of the symptoms which occurred during convalescence is obscure. Physical examination of the heart of patients who then exhibited tachycardia and dyspnea after exertion revealed no gross defects. Functional murmurs occurred, but afforded no guide as to the severity of the cases. It was quite apparent, however, that if muscular exercise was begun too early or pushed too far, a definite condition of irritable heart might be established which would persist for a long time. Neurasthenia sometimes entered into the clinical picture and care had to be taken not to let this condition obscure any definite abnormality which might be present.

An exceedingly striking feature in some patients with poisoning by lung irritants was the severe or even fatal symptoms induced by exercise. Some men who were apparently not severely gassed and who presented no notable symptoms would, after slight exertion, such as going to a meal or visiting the toilet, suffer a complete collapse, with dyspnea and cyanosis or even death, unless immediate treatment was instituted.

In cases which did not show an improvement after 72 hours, bronchopneumonia was generally found to be present. In these cases the temperature increased, reaching 38° to 39° C. An increase in the severity of the cough was noted, and the sputum assumed a more mucoid character. Numerous fine and coarse râles were heard on auscultation, and signs of lung consolidation were often present. Death might occur at any time, with symptoms of increased circulatory and respiratory insufficiency.

Frequently a striking improvement was noted in cases which had a very stormy onset and in which the condition had appeared most alarming. Occasionally even the most apparently hopeless cases made excellent recoveries. The pulmonary edema was gradually absorbed, the dyspnea improved, and the signs of interference with the circulation disappeared. The cough, however, frequently persisted for a considerable time. The expectoration changed in character from serous to mucoid or mucopurulent, entirely disappearing after a variable period.

On the other hand, the danger was not always removed after a favorable change had supervened. Secondary bacterial infections might occur to produce bronchopneumonia or, more rarely, lobar pneumonia, which threatened the life of the patient.

In a number of cases seen during the war, which at first gave the impression of being severe intoxications, further observation demonstrated that either physical or psychic shock was actually responsible for the condition. As the patient recovered from the shock the further train of symptoms showed that gassing was unimportant. In many cases shock which followed a severe wound made it difficult to determine the extent of gas absorption.

In the greater number of cases of gas poisoning the inhaled gas was of a low degree of concentration, it usually having been freely diluted by the air. Naturally, the greater the extent to which the offending gas had been diluted the milder were the resulting symptoms. Other factors naturally lessening severity of exposure were improvements in gas protection and additional precautions against inhalation, which were generally taken by officers and men after the serious results of gas poisoning were fully realized by them.

When poisoning occurred as a result of the inhalation of a gas of the lung-irritant group which had been greatly diluted the symptoms were much milder than those just described. The effects lasted for a shorter time, and the irritation of the eyes and upper respiratory tract was less severe. The lungs and bronchi were not affected, and if coughing was occasioned it was superficial and from irritation of the pharynx and larynx. The severe constitutional effects were entirely absent in these cases. Difficulty was experienced at times in differentiating intoxications of this character from conditions simulated by men who took advantage of the pretense of having been gassed to escape the dangers of the battle field. Yet, ascertaining whether a man had been gassed was of the utmost importance, for, as has been previously noted, in certain instances patients whose premonitory symptoms were mild developed most aggravated forms of gas intoxication. The majority of men who had inhaled the combat gases in mild concentration made prompt recovery and were returned to duty in a short time.

SYMPTOMS IN SPECIAL ORGANS

SKIN

In the higher concentrations many of the gases of the lung-irritant group caused mild inflammatory reactions of the skin of exposed parts, especially of the neck and of that portion of the face not covered by the gas masks. The inflammation was never of the severe type caused by gas of the vesicant group. The changes in the color of the skin were due to circulatory disturbance, vasomotor influence, and the altered composition of the blood.

EYES

The different gases included in the group under consideration (lung irritants) varied in the extent of their action on the eyes. Mild inflammations of the conjunctiva, with pain and flow of tears, were common, but erosion of the cornea and deeper structures did not occur unless there had been a direct application of the gas in a concentrated form. The eye symptoms were of so little importance in comparison with those involving the circulatory and respiratory systems that they were not often noted.

RESPIRATORY SYSTEM

When the exposure had been to gases in low concentration only, the upper part of the respiratory tract was involved and the symptoms were those of a pharyngitis or laryngitis. Following inhalation of gases in higher concentration, the alveoli of the lungs were most seriously involved. The resulting edema sometimes occurred promptly after the inhalation of the gas, but usually was not noted until a few hours later. The symptoms, described above, were the result of deficient oxygenation of the blood. With the onset of the edema an increase of

lung volume frequently occurred, and this emphysema kept pace with the increasing edema, later disappearing with the absorption of the fluid. Cough and expectoration were variable. When expectoration was present the sputum, on being collected, presented three distinct layers—an upper layer of froth, a middle serous layer, and a bottom layer which adhered to the container when the two upper layers had been decanted. This consisted of a mucilaginous liquid of the consistency of apple jelly, which might be rusty or streaked with blood.

Histological examination of the sputum revealed, during the first and shortest stage (first few hours), more or less modified epithelial formations from the bronchial tubes; during the second stage, in addition, débris from the epithelium of the lungs, leucocytes, and red corpuscles. The sputum in both these stages was noticeably free from pathogenic bacteria, only a small number of ordinary mouth saprophytes being present. Later, however, with the onset of pneumonic complications many organisms were found.

In some fatal cases with extensive edema expectoration did not occur, the patient dying before the edema fluid could pass from the alveoli into the bronchial tubes.

After the second or third day absorption of the fluid was rapid. In cases in which secondary infection set up a bronchopneumonia the symptoms were of this complication. In fatal cases of this character the lung changes frequently could not be differentiated from those occurring in the secondary bronchopneumonia following any of the infectious diseases.

CIRCULATORY SYSTEM

The lung-irritant gases are not believed to exert any direct physiological action on the heart. The disordered action of the heart which followed intoxication with a gas of this class was the result of the pathological changes occurring in the lungs and of the changes in the composition of the blood. As the obstacles to the circulation of the blood increased, the additional efforts on the part of the heart resulted in dilatation, first of the right side and later of the entire organ. This increase in size could be readily demonstrated by X-ray observations.

The first indications of interference with the circulation of the blood were cyanosis, paleness, blue lips, and signs of impaired circulation in the extremities. While at first the heart rate was little affected, as the condition of the patient became serious the pulse rate increased and the pulse usually became soft, rapid, and thready; the rhythm was rarely disturbed.

Physical examination of the heart was difficult in severe cases on account of the restlessness of the patient, the dyspnea, and the presence of large sonorous râles in the lungs. When the cardiac sounds could be distinguished, they were distant and uncertain and the respiratory movements had an abnormal influence on the cardiac rhythm. There was no indication of valvular lesions, but by reason of the cardiac insufficiency functional systolic murmurs might be heard. The end of the beat was marked by a rhythmic asystolia. Circulatory disturbances in severe cases were marked by a high degree of cyanosis, darkness of face and extremities, swelling of the jugular vein, enlarged liver, and decrease of the urinary secretion.

The blood pressure was subject to cyclic modification. In the early stages of the intoxication the blood pressure was decreased. Later it remained

low (the usual rule), but in certain exceptional cases the systolic pressure reached 200 mm. Hg. The reasons for these changes are not definitely understood.

Examination of the blood showed less change than might have been anticipated from the results of blood letting when a dark, sticky blood that left the vein slowly and coagulated quickly was obtained. The blood showed neither important chemical changes nor evidence of absorption of the poisonous gas. The hemoglobin retained its facility for absorbing oxygen, but frequently the oxygen content of the blood was below normal. The total volume of blood was considerably decreased on account of the exudation of blood plasma into the lungs as edema. There was no actual change in the number of red corpuscles or in the amount of hemoglobin, consequently a relative increase of these elements existed. The red cells numbered as high as 7,000,000 or 8,000,000 to the cubic millimeter, and the hemoglobin readings ranged as high as 140. The number of leucocytes appeared normal (7,000 to 9,000 per mm.), therefore, in view of the decreased blood plasma, an actual leucopenia must have existed. An important acceleration of blood coagulation occurred.

DIGESTIVE SYSTEM

Nausea and vomiting were often among the first symptoms noted. They probably were more often the result of reflex action from irritation of the throat rather than from the direct effect of the gas on the stomach, although at times the swallowing of poisonous material was responsible. Anorexia, a frequent symptom, was often noticed in the early stages and might be very protracted. Constipation was more frequent than diarrhea, but during the period of convalescence enterocolitis with diarrhea was encountered in some cases.

The liver was enlarged and sensitive. Only rarely was jaundice observed. Enlargement of the spleen was not uncommon.

NERVOUS SYSTEM

The nervous system was always involved. From the time of the first sensation of suffocation, immediately following intoxication, the patient seemed completely overcome with fatigue. Among the nervous symptoms noted were headache (marked by crisis when any exertion was undertaken), vertigo, staggering, muscular weakness, disturbance of tendon reflexes, nystagmus, numbness, and even unconsciousness. Mental torpor was characteristic of many cases, while in some severe ones restlessness was marked, with at times a low muttering semidelirium.

In fatal cases consciousness was usually maintained until the end. In patients addicted to the use of alcohol great excitement, delirium, and even hallucinations were not uncommon. The psychic element, which was prominent in many cases, was usually of a depressive nature, and during convalescence the hysterical and neurasthenic complexes were frequently in evidence. Neuritis and neuralgia were not noted as sequelae.

URINARY SYSTEM

These gases did not appear to have any selective action on the kidneys. In cases where suffocation and cyanosis were marked, there were signs of congestion of the kidneys. In the early stages of the intoxication the amount of urine was generally reduced, and transient albuminuria was not uncommon. In patients who recovered, the urine was usually normal after a few days.

BODY TEMPERATURE

Both the general and local effects exerted an influence on the body temperature. Febrile reactions were always in evidence. In mild cases the temperature reached 38° C. on the first day, but returned to normal by the third. When a complicating infection of the lung occurred the temperature rose to 38° or 39° during the first day, 38° to 40° on the following day, and remained between 39° and 40° for several days.

PHYSICAL SIGNS

In certain patients during the early stages of poisoning with the lung-irritant gases, no abnormal auscultatory or percussion signs could be discovered; there was simply an increase of the respiratory rate and an increased fullness of the pulse. In a well-developed case inspection showed labored respiration and cyanosis.

It is noteworthy that such physical signs as were detected at first were most marked over the upper lobes of the lungs, and not at the bases. The percussion note might remain resonant over the chest notwithstanding the existence of marked pulmonary edema. In many cases, however, the note was impaired, especially over the back. Local tympany might be found, resulting from emphysematous areas.

With the onset of the pulmonary edema the signs of this condition were elicited on auscultation—fine crackling râles, harsh and distant breath sounds, and not infrequently pleural friction rubs. As the edema increased resonance became impaired, and breath sounds were lost, being totally replaced by crackling râles or silent areas.

The heart dullness was increased to the right, and on auscultation the heart sounds were weak, especially the pulmonic second sound.

When bronchopneumonia supervened the physical signs were those of that disease.

PHOSGENE AND DIPHOSGENE

Phosgene and diphosgene are among the most intense lung irritants known, and are regarded as the most effective war gases of their type. The odor of these gases is perceptible in a concentration of 1 to 1,000,000, and they will cause death in men exposed to a concentration of 1 to 5,000 for 5 minutes, of 1 to 20,000 for 60 minutes, and even of 1 to 1,000,000 if breathed for a considerable length of time. In a dilution of 1 to 50, which it is rarely possible to produce for battle uses, one inhalation will cause death. It was in cases of poisoning by phosgene that the delayed action, mentioned above under the general symptoms, was most apt to occur. Lacrymation usually occurred, but cough was not a prominent symptom. Of the two types of cases, one with the "blue" cyanosis face, the other with the "gray" cyanosis, the gray type was more frequently observed, but many intermediate types were seen. Sometimes a patient who, in the early stages, had shown a congestive cyanosis, with a full pulse, would gradually assume a grayish pallor, the pulse becoming accelerated and weak.

Instances were not infrequently reported in which soldiers who had been exposed to phosgene were able to carry on their work for an hour or two with only trivial discomfort, and even to march from the trenches to their quarters,

then to show marked symptoms of intoxication and to pass into a state of collapse, with progressive edema of the lungs, which in some proved rapidly fatal. In such cases the ingestion of a heavy meal seemed sometimes to have a prejudicial effect. In other instances men who had passed through a gas attack and subsequently complained of only slight cough, nausea, and tightness of the chest while resting in the trenches, collapsed and even died quickly after attempting to perform some vigorous muscular effort several hours later.

A minor degree of the same delayed effect was sometimes seen when men who had been slightly gassed discovered, on trying to walk, that they became unusually tired and breathless, and in consequence were obliged to rest frequently. In these cases the deficiency of oxygen, the probable result of an already existing pulmonary edema, was not felt until muscular exertion increased the need for oxygen.

One very striking example of the delayed effect was observed in a patient who was carefully watched after only a brief exposure to a strong concentration of phosgene. The greatest care was taken to prevent any muscular exertion, so that no complicating factor was introduced. The immediate irritant symptoms and coughing that were produced during the exposure soon diminished when the patient was removed to uncontaminated surroundings. An hour and a half later there was no coughing and the patient seemed practically well, the pulse being normal. His condition remained very good until four or five hours after exposure to the gas, when he showed signs of cyanosis about the lips. Coughing then recommenced, with the expectoration of frothy sputum. Soon the face and lips became of a gray, ashen color, though the pulse remained fairly strong. About 4 pints of clear, frothy, yellowish liquid was coughed up in the next 75 minutes, and at the end of this time he died. At no time was there any marked struggle for breath, nor did the patient realize how ill he was.

CHLORINE

A much stronger concentration of chlorine is required to cause severe pulmonary edema, or even lacrymation, than is the case with phosgene. In a concentration of 1 to 100,000 chlorine is perceptible, a strength of 1 to 50,000 causes inconvenience, in a dilution of 1 to 1,000 death results after exposure for five minutes.

Chlorine is far more irritant to the respiratory passages than is phosgene. A very marked feature in the early gas attacks, when chlorine alone was used, was the paroxysmal and violent coughing, which not only occurred during the exposure but persisted for a long time afterwards. Emphysematous changes were pronounced and submucous emphysema of the neck and chest occurred in a number of instances. As a general rule these patients exhibited deep cyanosis rather than pallor and collapse, with a fairly full pulse and marked dyspnea. Copious frothy expectorations was common. The gastric symptoms were often marked, vomiting frequently being an early symptom.

Delay in the onset of serious symptoms was not evident in chlorine poisoning. Though exudation of fluid into the lungs perhaps did not start at once, the violent paroxysms of coughing, the pain, the dyspnea, and the repeated attacks of vomiting from the first conveyed the impression that the patient was seriously ill.

CHLOROPICRIN

This gas occupies a position midway between phosgene and chlorine in respect to its efficacy as a combat gas. To produce severe pulmonary edema chloropicrin must be used in decidedly higher concentrations than phosgene, but it is much more deadly than chlorine. It is a stronger lacrymatory agent than phosgene, though inferior in this respect to the true lacrymators. Pain in the chest and epigastrium, abdominal discomfort, and violent attacks of vomiting were exceptionally marked. Brief exposure to a strong concentration in some instances caused temporary unconsciousness.

Unlike phosgene and chlorine, chloropicrin had a cumulative action. Frequent exposures to small doses of chloropicrin, each of which would have only a trivial effect in itself, would gradually lead to a greatly increased susceptibility to this gas. A man who had acquired this susceptibility was liable to attacks of "asthma" whenever he had been exposed to a trace of chloropicrin in the air. The attacks usually occurred at night and were characterized by the sudden onset of a rapid, shallow type of respiration associated with a feeling of tightness of the chest and a sense of suffocation which caused considerable distress. There was usually a short, dry cough at intervals, which was occasionally followed by the expectoration of a small quantity of tenacious mucus. The attacks lasted for as long as two hours and resembled, though exaggerated, the attacks of nocturnal dyspnea, described as occurring during convalescence from poisoning by lung irritants.

NITROUS FUMES

As regards the production of pulmonary edema, nitrous fumes are perhaps somewhat less toxic than chlorine. The great danger of nitrous fumes arose from the fact that in the concentration usually met with there was comparatively little sensory irritation of the eyes or upper respiratory passages, and in consequence a man working in such an atmosphere would not recognize its deadly nature. Air which contains enough nitrous fumes to cause irritation to the nose or air passages must be regarded as very dangerous.

Delay in the onset of acute symptoms was pronounced unless the concentration of the gas was high, when fatal asphyxiation might ensue rapidly. As a rule a quiet period of four to eight hours elapsed after exposure, during which time the patient usually felt quite well and had no hesitation in performing his usual routine tasks, or in eating a hearty meal. After this, symptoms of acute pulmonary edema frequently developed with alarming rapidity, death often ensuing in a few hours.

VESICANTS

The gases of the vesicant group exert an intense effect on the skin and eyes, also on the respiratory tract as well when inhaled. The extent of inflammatory reaction produced in the skin varied with the strength of the gas and the duration of the exposure. Skin lesions which followed exposure to these irritants varied from simple erythema to burns of the second or third degree. Conjunctivitis, of varying degree, was the usual type of eye involvement, although keratitis occurred in the more severe cases. All degrees of inflammation might be present in the respiratory tract, from a simple hyperemia to a necrosis of the mucous membrane.

DICHLORETHYLSULPHIDE (MUSTARD GAS)

Dichlorethylsulphide (mustard gas) was the only gas of the vesicant group which was used on a large scale during the war; for this reason, the symptomatology given below is based on observation of the effects of this gas.

The effects of mustard gas were not experienced for several hours after exposure. While it has a characteristic odor, it is toxic in concentrations which can not be detected by the sense of smell. Soldiers might be exposed for several hours, therefore, to mustard gas of sufficient concentration to cause serious results without being aware of the fact. Furthermore, the action on the skin was at first painless, and the presence of the gas could not be detected in this way.

The effects of mustard gas depended largely upon whether the liquid or vapor was encountered and upon the concentration of the gas in the latter case. Exposures may be roughly grouped into three classes: (1) to liquid; (2) to vapor of high concentration; (3) to vapor of low concentration. The liquid penetrated clothing and leather in a very short time and produced severe blistering. Such cases usually resulted from direct splashes of shell bursts, or from sitting or lying in places covered by the liquid.

Vapors of high concentration penetrated clothing rather quickly and sufficiently to cause general irritation of the skin. Without mask protection, serious lesions of the eyes, throat, and lung resulted.

Vapors of low concentration, with brief exposure, might result in nothing more than insignificant irritation of the moist surfaces of the body or in slight conjunctivitis, but when a long exposure was sustained, the same results were to be expected that were produced by a vapor of high concentration.

British field experimentation showed that severe eye effects, involving incapacitation, might follow exposures of:

Concentration	Time of exposure
1 to 100,000.	3 to 5 minutes.
1 to 1,000,000.	1 hour.
1 to 5,000,000.	6 to 12 hours.
1 to 10,000,000.	12 to 24 hours.

The sense of smell became fatigued soon after entering a vapor of low concentration, and this, together with indifference to the presence of such area contaminations on the part of inexperienced troops, resulted in many skin and eye casualties. Dichlorethylsulphide, as a general rule, was fired at night so that its odor was apt to be disregarded by many on the following day. The sun was counted on to slowly vaporize the gas during the ensuing days and to produce results.

GENERAL SYMPTOMS

The effects of mustard gas varied widely according to the concentration, the period of exposure, and the susceptibility of the individual. It was found that many persons had what might be regarded as an immunity against certain concentrations of the gas and could pass through exposure to such concentrations without ill effect. On the other hand, a marked idiosyncrasy to its action was noted in certain individuals.

Occasionally nausea, retching, vomiting, and smarting of the eyes occurred as early as from 20 to 60 minutes after exposure; they were of great value in warning of the presence of the gas. Usually, however, symptoms did not appear until from two to six hours after exposure. Nausea, vomiting, a sense of fatigue, and headache were then noted. The eyes were inflamed and lachrymation, blepharospasm, and photophobia were present. A watery discharge ran from the nose and sneezing was frequent. The face and neck became red, and signs of pharyngitis and bronchitis appeared. The pulse and respiratory rate were increased.

The symptoms mentioned increased in severity, and by the end of 24 hours the face, neck, hands, inner surface of the thighs, genitals, and buttocks were acutely inflamed, vesication frequently being present. One of the most distressing symptoms was pain in the eyes, which might be very severe. The patient was virtually blinded, with tears oozing from between the bulging, edematous eyelids, over his reddened and slightly blistered face, while there was a constant nasal discharge and an occasional harsh, hoarse cough. Widespread and severe inflammation of the mucosa of the upper respiratory tract might be present, and the expectoration was then thick and blood tinged. Practically never did death occur during the first day. During the second day the condition of the patient grew progressively worse. Large blisters formed on the skin surface involved, while the scrotum and penis were swollen and edematous. The bronchitis became fully developed, with abundant expectoration of mucopus in which might be found large necrotic sloughs from the tracheal and bronchial mucous membrane. Cough was severe, and temperature, pulse, and respiration were increased.

After this, bronchopneumonia, the result of secondary infection, frequently developed rapidly, with marked coalescence of the involved areas. The patient was usually delirious, coughed and expectorated frequently, and complained of severe pain; cyanosis was marked. After a varying period he lapsed into unconsciousness and died, or recovery might set in. Death occurred from the end of the second day to as late as the fourth week after exposure.

The description given above is that of a severe case. When lower concentrations were encountered the patient usually escaped with a mild pharyngitis or bronchitis, if the gas was inhaled; the action of the gas was frequently exerted locally on the skin without involvement of the respiratory tract. In the latter case the skin lesions were those described later in this chapter.

Patients who developed severe bronchopneumonia usually died; those not so severely gassed eventually made a good recovery. Signs of improvement might appear at any time during the progress of the illness, and the period of convalescence depended on the severity of the local lesions. Photophobia usually persisted for a long time after the local inflammatory changes had disappeared. The bronchitis, also, was frequently persistent, and complaints of substernal and epigastric pain were made. Residual complaints were frequently of psychic origin. It is very doubtful whether severe sequelæ occurred in those recovering from poisoning by dichlorethylsulphide; this subject is considered in a later chapter.

Properly used, well-fitting gas masks generally prevented the inhalation of mustard gas in sufficient quantity to cause pulmonary symptoms, but, of course, had no effect in preventing the skin lesions resulting from contact with the gas.

SYMPTOMS OF SPECIAL ORGANS

SKIN

The cutaneous effects of mustard gas were caused by direct contact with the liquid or by the vapor which, in addition to affecting exposed parts, was diffused through the clothing. The distribution of the consequent injury varied accordingly. Certain areas of the skin, particularly parts where moisture and sebaceous excretions are excessive, were much more sensitive to the irritant action. The hardened skin of the palms of the hands and soles of the feet was much less affected than that of such parts as the crotch and genital organs.

The skin lesions may be classified, according to severity, as follows: 1. Erythema, which usually involved the face, neck, and chest; the axillæ and flexure of the elbows; the inner surfaces of the thighs; and the scrotum and penis. This might appear in from 2 to 48 hours, or be delayed, either locally or generally, for several days. This condition resembled the erythema of scarlet fever, but was frequently accompanied with slight swelling and a mild burning sensation and itching. This erythema disappeared in a few days without leaving any trace or passed into the next type. 2. Very superficial blistering over the same areas, either in small vesicles or large blebs, which developed as painless collections of yellow or reddish serum just beneath the epithelium. If the covering was removed, a raw, moist surface was exposed, and secondary infections of these areas led to severe tissue destruction. This was particularly frequent in blisters of the scrotum and penis. The blisters usually appeared on the second day, but there might be an outcrop even as late as the second week after exposure, long after the patient had been carefully cared for and his clothing had been changed. 3. Staining of the skin with a dark brownish-purple tint, usually in areas that previously had been erythematous. This staining was of no consequence and disappeared in a few weeks with desquamation.

The more severe skin lesions following exposure to mustard gas (that is, the lesions similar to burns of the second or third degree) were always the result of secondary bacterial infection. In some instances these severe lesions ran a protracted course, and a considerable degree of scarring resulted. It was the impression at first that the contents of the skin blisters would cause an erythema of uninvolved skin, but apparently this was disproved later.

An interesting observation made during the war was that men, without exception, who permitted the hair on the head to grow long and who were subjected to mustard-gas exposure had the most severe symptoms. This was due to the fact that this shaggy growth of hair afforded an excellent place for harboring the gas.

EYES

Conjunctivitis of sufficient intensity to incapacitate those exposed to mustard gas usually developed in from 2 to 48 hours. When very low concentrations of the gas had been encountered, the resulting conjunctivitis was mild and might develop only after several days had elapsed. In severe cases the patients were temporarily blinded by swelling and spasm of the eyelids. In a case of ordinary severity the first symptoms to appear were of a subjective nature and were noticed from two to six hours after exposure. The patient complained of a feeling of pressure on the upper eyelids, a feeling like that of

a foreign body in the eye, slight burning and tingling; he avoided light, and had increased tear production. Profuse lachrymation, with pain and headache followed. By the second day the lids had become swollen, the conjunctiva was markedly congested, a mucopurulent discharge was present, which frequently adhered to the edge of the lids, gluing them together and causing scab formation. The cornea at times became steamy, especially in the line of exposure, but actual ulceration was rare.

The conjunctivitis cleared up quickly and usually the injection disappeared in less than a month. But the inflammation was liable to be succeeded by photophobia which, if improperly treated, delayed the patient's return to duty even as long as two or three months. This condition was apt to assume a neurasthenic character and irritation was sometimes maintained, consciously or unconsciously, by frequently rubbing the eyes. In such cases it was found that the ocular conjunctiva opposite the lower lid was red while the conjunctiva above was normal.

Serious eye complications resulted from secondary infections. Even in the very severe cases of uncomplicated mustard gas, conjunctivitis cultures from the eye discharge rarely yielded any organisms other than saprophytes of the conjunctival sac.

RESPIRATORY SYSTEM

The effects of mustard gas on the respiratory tract depended on the concentration of the gas inhaled and the length of time exposure lasted. The nasal mucous membrane was involved to a less degree than the remainder of the tract, but even here a profuse watery secretion resulted which might later become purulent and contain sloughs. Actual ulceration was rare. In the more severe cases epistaxis was common.

Inflammation and erosion of the posterior pharyngeal wall sometimes was sufficient to interfere with swallowing. Laryngoscopic examination revealed redness and swelling of the mucous membrane and sometimes of the false vocal cords. Edema of the larynx was present, but was never sufficient to necessitate tracheotomy. Ulceration occurred after exposure to high concentrations. Hoarseness was rare, but exposure to low concentrations frequently caused laryngitis and some aphonia, even when the conjunctiva was not involved. Severe pain in the throat, with cough, was often complained of and disturbed the patient's rest at night.

In mild cases the trachea and bronchi were only slightly affected. In severe cases there was an extreme inflammation of the mucous membrane, with extensive necrosis. Death was usually the result of bronchopneumonia caused by secondary bacterial invasion; in extremely severe cases, however, it might be caused by asphyxia due to the blockage of the air passages by large pieces of displaced sloughing membrane. When bronchopneumonia developed, the symptoms were of that disease. The characteristic pulmonary edema of the lung-irritant gases was not present in intoxications with the vesicants.

DIGESTIVE SYSTEM

The early vomiting rarely persisted for more than a day, and the epigastric pain disappeared in a short time. Hematemesis was exceedingly rare. There were no lasting effects in the stomach, and the intestines were never affected.

CIRCULATORY SYSTEM

The blood was unaltered and the heart was unaffected, except by the changes associated with the pulmonary infection. During early convalescence some patients complained of fatigue after exercise and shortness of breath, associated with precordial pain and tachycardia. These symptoms were chiefly due to a nervous debility, and yielded promptly to tonics and graduated exercise under firm discipline. Secondary anemia sometimes was noted after a severe and chronic illness.

URINARY SYSTEM

Albuminuria was reported in the first 24 hours (in cases of early fatality), but was not found at a later date. Very rarely, acute hemorrhagic nephritis was observed. Pain during micturition and even retention of urine occasionally resulted from the edema and blistering of the penis.

LACRYMATORS

Various bromine compounds, notably benzylbromide, were used for their lacrymatory effect. They were not often used by themselves, but generally with or as preliminary to an attack with lung-irritant gases. The irritant effect of lacrymators on the eyes and upper respiratory tract rendered it extremely difficult for the men affected by them to properly wear their gas masks; thus they were rendered easy victims to the lethal gases which were to follow. The lacrymators were used also in gas chambers for purposes of instruction and to test the fit of gas masks.

The lacrymator gases caused acute irritation of the eyes, with profuse lacrymation, thus producing a temporary functional blindness. This did not last long, and after the immediate effects had passed away the man was ready for full duty.

STERNUTATORS

The sternutator or "sneeze" gases, of which diphenylarsine was one of the chief, exerted their action on the nose and pharynx.

The symptoms, and these appeared immediately after inhalation, were sneezing, coughing, sinus and substernal pain, headache, increased flow of saliva, and frequently nausea and vomiting. While these were most disagreeable, they were never of serious import and complete recovery occurred in a few hours.

CARBON MONOXIDE

Carbon monoxide was not used as a combat gas, but during combat activities casualties frequently occurred as the result of inhaling it. Carbon monoxide was generated by the detonation of high explosives, as when considerable firing took place from an improperly ventilated emplacement, and also by fires in dugouts. By the detonation of 1 kg. of modern high explosive from 600 to 800 liters of carbon monoxide are evolved. Carbon monoxide is lighter than air; consequently it diffuses rapidly in open spaces, and fatalities in such places are rare. On the other hand, within closed areas, as trenches and dugouts, dangerous concentrations frequently occurred, and these resulted in numerous casualties.

Carbon monoxide, which is odorless and colorless, owes its poisonous action to the fact that it combines with the hemoglobin of the blood to form

a dissociable compound, and thereby takes the place of oxygen. If, therefore, a small proportion of carbon monoxide is present in the air breathed, the hemoglobin in the blood will divide itself between the two gases, the final partition being determined by their relative concentration. The oxygen-carrying properties of the blood are properly diminished as the hemoglobin becomes more and more saturated with carbon monoxide.

Gas masks were useless against this type of gas. Mine-rescue apparatus or similar protective oxygen apparatus afford protection when properly used.

Carbon monoxide causes asphyxiation, with symptoms of vomiting, giddiness, semiparalytic weakness, acceleration of the pulse, shallow, irregular, and jerky respiration; and, finally, dulling of the sensibility, which may pass into complete unconsciousness, with widely dilated insensitive pupils, general functional failure, and death. Mental confusion frequently occurred, and in slight cases only headache was complained of; sometimes this is accompanied with nausea or the patient might appear to be madly intoxicated.

Except with massive doses, when loss of consciousness was rapid, the symptoms developed gradually as the gas was slowly absorbed. The demand for oxygen by the individual was important in determining the rapidity of the poisonous effect. In a man at rest in a concentration of the gas of 1 part in 1,000 it would be about two hours before definite symptoms appeared, and he was not disabled until after a lapse of two and a half hours. Muscular work accelerated symptoms.

The symptoms might remain stationary at any stage, since the degree of saturation of the hemoglobin with carbon monoxide had reached a final point which was determined by the relative concentrations of the carbon monoxide and the oxygen which were simultaneously trying to combine with the hemoglobin.

TREATMENT

The successful treatment of gassed patients depended on early recognition of the condition, removal of the patient from the gassed area, determination of the type of gas responsible, and prompt application of the necessary therapeutic measures. Many who were affected by the lacrymators or sternutators, as well as mild cases of mustard-gas poisoning, were promptly returned to duty, while others required longer or shorter time.

If gas was still present in the area where the patient was first seen, the good fit of his mask was verified, and care was taken to see that it was properly applied. If the mask was broken or did not fit properly, a new one was adjusted. Then, at the earliest possible moment, all gas casualties were evacuated from the contaminated area. Strict orders were in force that no patient affected by the lung-irritant gases be permitted to walk or to indulge in undue exertion of any character. Such patients, as already explained, were always transported. Similar precautions were taken with patients who had inhaled mustard gas, although, as has been noted, the danger from exertion was not so marked in this type of gas poisoning as in poisoning with gases of the lung-irritant group.

When no gas was present in the area at the time the patient was discovered, an ether pearl was administered if he was dyspneic or coughing. This was repeated in 5 minutes, again in 10 minutes, and thereafter every 15 minutes, until the dressing station was reached. When indicated, artificial respiration

by the Schaeffer method was practiced. While being conducted to dressing stations patients were kept in the open so far as possible, and later on, the doors of ambulances carrying gassed men remained open.

Oxygen was administered to and venesection performed on patients whose condition so indicated (lung-irritant gases) at first-aid or dressing stations where the necessary facilities were available. From the dressing stations patients were conducted to the triage or collecting station; in some divisions the dressing station also functioned as the triage.

In mild cases of mustard-gas poisoning, however, the patients were conducted to a dressing station where they were bathed and furnished with a change of clothing. They were then transferred to a gas hospital for further treatment.

At the triage, cases of gas poisoning and suspected poisoning were examined by a medical officer, especially skilled in the diagnosis of this condition (usually the division gas medical officer or his assistant), and those not gassed were separated from the gassed patients. A distinction between those affected by the different types of gases was made, and the various patients were transferred to suitable gas hospitals or to hospitals equipped for the care of gas cases.

Upon arrival at a division gas hospital patients were classified according to the type of gas to which they had been exposed and then by the severity of their symptoms. The slightly gassed and doubtful cases of gassing were placed in an observation ward for a few days, at the end of which time they were usually ready for return to duty. The more severe cases were assigned to the proper ward and then were either retained temporarily in the hospital or were evacuated to corps or army gas hospitals located farther to the rear, as determined by their condition.

At all places where the clothing of sufferers from mustard gas was removed, facilities were provided for the immediate degassing by appropriate methods of all articles of wearing apparel. Especial care was taken by all attendants coming in contact with these articles and gloves were always worn.

LUNG IRRITANTS

The first indication was removal from the gassed area. If this was not possible for any reason, a well-fitting gas mask was properly applied. In any event, at the earliest possible moment the patient was transported into uncontaminated atmosphere. While moving such a gas casualty in an ambulance, provision was made for an inflow of air, the windows being left open.

The treatment of poisoning by gases of the lung-irritant group comprised the following measures: (1) Rest, (2) warmth, (3) venesection, (4) oxygen inhalations, (5) cardiac stimulation, (6) fresh air, (7) inhalation of ether, (8) regulation of diet.

Rest.—Rest at all times was essential, and the nearer this approached absolute rest the better. The lack of a sufficient supply of oxygen in the circulating blood, consequent upon the pathological changes in the lungs, was the main factor in the production of the serious symptoms attending this type of gas poisoning. As is well known, the oxygen requirements of the human organism are largely dependent on the amount of work being done by the body muscles. Physical effort of any sort greatly increases the demand for oxygen by the tissues of the body. For these reasons every effort was made to prevent seriously gassed from making any unnecessary exertion.

These patients were always regarded as litter cases and were transported as little as circumstances permitted. Usually the clothing was not removed until they had been admitted to a hospital where they could be retained for treatment. They were not bathed until they had been sufficiently rested. Even in cases progressing favorably, rest in bed was enforced for several days.

Warmth.—Warmth was regarded as important. Cold caused an increased demand for oxygen. Heat was provided by methods similar to those adopted for the treatment of shock.

Venesection.—This was a matter of routine treatment and was performed as early as possible if the patient was at all dyspneic or cyanotic. Even at the first-line dressing stations venesection was performed when indicated. It was frequently necessary to select a large-sized vein and to incise it freely or to excise a portion of the vein wall, as the blood was inspissated, clotted quickly, and flowed with difficulty.

For practicing venesection, two different methods were adopted. Usually from 250 c. c. to 600 c. c. of blood were withdrawn, and if necessary this was repeated in a few hours. The other method involved the removal of about 250 c. c. of blood every three or four hours during the first day. The patient stood the removal of this amount of blood at such intervals without harm. Some observers believed that these repeated withdrawals of a small amount of blood were more efficacious than a single bleeding of a larger quantity. The majority were of the opinion that venesection was contraindicated in patients who were in the ashen-gray type of asphyxiation, although some reports indicate that the results of bleeding proved most gratifying even in this class of patients. Venesection performed later than during the first 18 hours after gassing was not appreciably beneficial.

Oxygen inhalation.—The administration of oxygen to all dyspneic, cyanotic patients was of vital importance. Under its influence the cyanosis often disappeared temporarily, and the respiration was quieted. Oxygen was given by means of a face mask equipped with in-and-out valves in such a manner that the patient received a mixture of about a 40 per cent oxygen. The oxygen was administered as continuously as possible up to the point of disappearance of the cyanosis, and was repeated whenever indicated. Rectal, subcutaneous, and intramuscular injections of oxygen were also tried, but were not found advantageous.

Cardiac stimulation.—If the heart action indicated cardiac weakness, stimulants were given. Camphor, sparteine, and caffeine were found beneficial. Digitalis was used by some medical officers, but others objected to its use on account of the slowing of the heart action.

Fresh air.—The desirability of an ample supply of good air has already been mentioned in connection with transportation. For the relief of the sub-sternal pain, especially in inhalation of ether, a few drops of ether held before the patient's nose on a piece of gauze and inhaled by him was found to be satisfactory. Alcohol or spirits of menthol used in the same manner also gave relief.

Sedatives.—Pearls of ether and ipecac, administered every one-fourth hour, were used at the front for their immediate sedative action. Cough was allayed and respirations made more regular. The emetic action of the ipecac unloaded the stomach, lowered arterial tension, and prevented pulmonary congestion.

Camphorated oil, caffeine, and emetine hydrochloride were found beneficial.

Regulation of diet.—The selection of a proper diet for the first 48 hours was very important. Food seemed to stagnate in the stomach, probably on account of the intense passive congestion of this organ, and caused distension, pressure on the diaphragm, and interference with the action of the heart. Deaths were observed which were apparently attributable to this cause, and accounts were numerous of men, gassed in the trenches, who had gone about their duties with no great discomfort only to fall dead at a meal several hours later. For this reason it was considered advisable to limit the diet for the first 48 hours to small amounts of well-diluted milk and then to permit a gradual increase of food. No restrictions were placed on the water intake.

Contraindications.—Opium in any form, atropine, adrenalin, the expectorants, and depressants, such as the coal-tar derivatives, were found to be harmful. Opium and its derivatives tended to check cough and hence to drown the patient in his own secretions. Smoking by gassed patients was prohibited, and convalescents were not permitted to smoke in wards containing acute cases. Digitalis and digitalin retarded heart action. Adrenalin increased pulmonary edema. Morphine should be given only in cases of extreme agitation. Inhalations of ammonia contraindicated because of the toxic action of chloramine which is formed when ammonia combines with chlorine.

Prevention of secondary infections.—In order to prevent the secondary pulmonary infections and complications of gas poisoning, which were so frequently attended with fatal results, care was taken to see that the patient was kept warm in a dust-free, well-ventilated ward and that careful nursing was provided. Especial care was taken to cleanse the mouth and teeth, particularly of unconscious patients. Exposure to cold of patients having bronchopneumonia was avoided.

Convalescence.—In general, gassed patients made rapid recoveries. The chief exceptions to this rule were those who developed secondary infections or those in whom cardiac symptoms appeared. Patients of the latter class often proved a most difficult problem to the medical officers in charge. They required constant observation for some time, especially those who, while usually appearing quite normal, developed severe attacks of dyspnea after physical exercise.

Graduated exercise was started after patients had been out of bed for from three to five days. Such exercise not only proved directly of benefit but also served as a valuable index of progress toward recovery. The first exercise was a moderate walk of a few hundred yards; and if no signs of breathlessness or undue increase in pulse rate were noted, longer walks were prescribed for each succeeding day. If at any time evidence of dyspnea or tachycardia appeared, all exercises were stopped for a few days and then gradually commenced again.

The most satisfactory treatment for the breathlessness and increased heart action was the routine administration of small amounts of oxygen. Camphor or caffeine, administered hypodermatically, and in severe cases, digitalis, were used with good results in these conditions.

VESICANTS

Soldiers who had been exposed to mustard gas were evacuated from the contaminated areas as promptly as circumstances permitted. If signs of

respiratory involvement were present, they were not allowed to walk, but were transported on litters or in ambulances, although the evil effects of exertion were not so marked in cases of this type of gas poisoning as in that where the lung irritants were responsible. In the care of patients with respiratory symptoms, all the precautions previously mentioned in connection with lung irritants were taken and, in addition, the clothing was entirely removed and the men were thoroughly bathed with soap and water at the earliest opportunity, care being taken to prevent chilling. After the bath, clean clothing was supplied. In mustard-gas poisoning it was not permissible to provide undue warmth until the clothing had been removed, as heat favors the diffusion of this gas.

Soldiers who had been exposed to mustard gas, but who showed no signs of pulmonary irritation, were conducted to the nearest station with the proper equipment close to the front lines, where they were thoroughly bathed and given a change of clothing. Bathing and change of clothing were usually accomplished at dressing or sorting stations.

The hair was clipped short. Observation of numerous cases demonstrated that long hair harbored the fumes of mustard gas and was instrumental in affecting the eyes, as well as increasing the irritation of the respiratory tract, besides the effect on the skin already mentioned.

SKIN

No attempt was made to remove the liquid gas from the body by means of gauze or other swabs before bathing. Such an action would have resulted in spreading the liquid over a wider surface, thus causing additional skin involvement. Efforts were made to find some agent which would neutralize the action of mustard gas on the skin. Alkalies were found to be valueless, and oxydizing agents, such as chloride of lime or potassium permanganate, were useless unless applied within a very short time. Chloride of lime was used both in the dry form and as a paste and, if applied within one or two hours after exposure, gave satisfactory results. The paste, however, could not be allowed to remain on the skin for longer than three or four hours, as it was itself irritant and corrosive. The central laboratory of the American Expeditionary Forces advocated and provided dichloramine-T in 5 per cent solution in an oily base. This substance liberates chlorine and was much less irritant than chloride of lime. Like the other oxydizing agents, it was of benefit only to patients who could be treated early. The ideal procedure for the cleansing of the skin proved to be thorough washing with soap and water.

When blisters had formed they were opened with surgical precautions; the fluid was taken up on gauze and not permitted to touch the neighboring skin. Skin erythema was treated with an alkaline dusting powder (talc, magnesium carbonate, zinc oxide) or by oily dressings such as petrolatum or paraffin. An excellent dusting powder, which was in general use, consisted of 200 grams each of calcium carbonate, magnesium carbonate, and zinc oxide, and 400 grams of talcum powder. For desquamated areas, especially the scrotum, zinc oxide ointment was used. Ambrine was found very satisfactory in treating the deeper burns.

When secondary infection had supervened in the burns the following wet antiseptic dressing gave good results: Zinc sulphide, 35; copper sulphide, 10; camphor water, 1,000. This was diluted with 9 volumes of water before use. Boracic acid compresses were also used. These dressings were continued until suppuration had ceased, when mildly antiseptic ointments were used.

Heliotherapy was reported as being of assistance in the disinfection and cicatrization of the more severe burns.

Coal oil or kerosene as an early wash was used extensively in France with good results, this procedure being followed by a hot bath with alkaline soap.

While dichloramine-T prevented to a great extent the development of erythematous areas around the vesicles, it did not prevent the damage already done to the skin. When used as a treatment for gas burns, the affected parts were kept moist with a 1 per cent solution in a 0.5 per cent solution of sodium chloride applied on lint.

Dakin solution in mild cases proved very satisfactory. The parts were either washed with the solution or, if possible, were immersed for two to three hours in a solution of a strength of about 0.5 per cent hypochlorous acid. If much of the body surface was burned, the solution was used as a bath, and for lesions of the genital organs a sitz bath was employed.

Of the many ointments used, the butyl salicylate ointment contained 20 to 60 per cent anhydrous wool fat and 25 per cent water proved to be very satisfactory, especially in relieving the troublesome irritations so often present.

The Italian ointment was also used extensively during the latter days of the war. This ointment consisted of the following:

Manganese linoleate.....	Grams 50
Zinc linoleate.....	500
Linseed oil.....	500

This ointment, if applied to the skin immediately after contract with mustard gas, prevented the formation of blisters.

EYES*

The eyes when affected required frequent irrigation with warm boric-acid solution or with 2 per cent sodium bicarbonate solution, followed by the instillation of liquid paraffin. Castor oil, while more irritating than paraffin, was often used if the latter was unobtainable. If the cornea was involved, sterilized atropine ointment of 1 per cent strength was substituted for the paraffin and repeated sufficiently often to keep the pupils dilated. While some hospitals used a 1 per cent solution of cocaine to relieve pain, the general opinion was that cocaine should not be used on account of its harmful effect on the cornea. If the discharge from the eye became mucopurulent, a weak solution of argyrol or protargol was used once a day. When the acute inflammation had subsided a weak solution of zinc sulphate was frequently employed as eyedrops.

The eyes were protected from the light either by darkening the ward or by the use of eye shades. Bandages were not permitted, as they helped to retain the discharges in the eyes. The patients were encouraged to pull the lids apart in order that the discharge might flow freely.

RESPIRATORY TRACT

Little could be done for symptoms due to irritation of the respiratory tract beyond controlling the violent coughing. For this purpose morphine was sometimes used, but heroin and dionine were regarded as preferable. Relief for the laryngeal irritation was obtained by the inhalation of steam saturated with menthol or benzoin. In the hospital treatment of patients who had inhaled mustard gas, of principal importance were measures to prevent secondary infection and the ensuing bronchopneumonia. These included care-

* The more severe burns of the eye, requiring attention by the ophthalmologist, are discussed in Vol. XI, Pt. II, Secs. III and IV, of this history.

ful nursing; adequate ventilation, obtained by open windows, and ample floor space per patient; ward cleanliness; avoidance of dust; and sufficient warmth.

The treatment of a supervening bronchopneumonia was conducted along the lines indicated for that disease, the patients being removed to a separate ward and cubicle.

Diet.—Patients with respiratory symptoms of mustard-gas poisoning were kept on a light diet on account of the intolerance for food that was usually manifest. The routine diet adopted for phosgene cases appeared to be the safest, namely, milk and water for 48 hours after exposure, then light diet, to which meat and vegetables were added as the patient's condition permitted.

LACRYMATORS AND STERNUTATORS

The effects of the lacrymators and sternutators, while most disagreeable, were not severe, and they usually passed off in a few hours.

For the relief of symptoms caused by the eye irritants the best treatment was found to be an eyewash of 14 per cent saline solution or 22.5 per cent sodium bicarbonate solution. A 1 per cent solution of cocaine was used when necessary to relieve pain.

For nasal irritants a 1 per cent cocained vaseline was applied to the nostrils. In case vomiting was a symptom, solution of magnesia was given internally.

CARBON MONOXIDE

As the symptoms caused by the inhalation of carbon monoxide are due to the gradual diminution of the oxygen-carrying power of the blood, it is clear that any increase in the oxygen demand on the body must be avoided. Therefore, absolute rest was one of the important factors in the treatment of carbon monoxide poisoning. The patients were not permitted to walk, but were transported by litter or ambulance. Fresh air was also essential, though not cold air if avoidable. When the patient was removed into an uncontaminated atmosphere the carbon monoxide gradually separated from the hemoglobin of the blood, and the hemoglobin resumed its normal function as an oxygen carrier. The removal of carbon monoxide from its association with the hemoglobin was greatly hastened by the administration of oxygen. It was regarded, therefore, as important to begin the administration of oxygen as soon as possible after the patient had been removed to a gas-free atmosphere. The administration of oxygen was continued from a half hour to an hour, depending on the severity of the symptoms. If the respiration was very shallow the administration of oxygen was often combined with artificial respiration. Collapse was combated by external warmth and friction of the limbs.

While in cases of poisoning with the lung irritants the interference with the gaseous exchange between the blood and the air in the lungs, consequent upon the pulmonary edema and the pathological changes in the lung tissue, often persisted for some time and necessitated the administration of oxygen for several days. In carbon monoxide poisoning the structure of the lung tissue was not damaged and oxygen was administered only with the intention of accelerating the discharge of carbon monoxide from the blood. After this had been accomplished there was no need of continuing the oxygen, as the oxygen-carrying power of the blood had become normal again. Any symptoms that persisted were due to the effects produced while the blood was charged with carbon monoxide and were unlikely to be influenced by the further administration of oxygen. Further oxygen administration was required, therefore, only if cyanosis began to develop subsequently as a result of secondary cardiac or respiratory failure.

CHAPTER VIII

STATISTICAL CONSIDERATION OF GAS CASUALTIES

GAS CASUALTIES ^a

The important rôle played by the combat gases during the World War is clearly shown from the casualty tables compiled in the Office of the Surgeon General. The total number of Army officers and enlisted men injured in battle was 224,089, of whom 70,552, ^b or 31.49 per cent, were reported as victims of gas poisoning. There were 13,691 deaths resulting from all battle injuries treated, of which 1,221, or 8.92 per cent, were attributed to the effects of the war gases. Tables 1 and 2 show the admissions to hospitals by divisions and by months of occurrence for gas casualties. The case mortality from the various kinds of gas is shown in Table 3.

TABLE 1.—*Admissions for gas poisoning, by organization, American Expeditionary Forces. Absolute numbers and percentages of total number* ¹

Organization	Number of admissions ²	Percent- age of total	Organization	Number of admissions ²	Percent- age of total
1st Division.....	5,676	8.05	76th Division.....	7	0.01
2d Division.....	2,229	3.16	77th Division.....	2,875	4.08
3d Division.....	3,894	5.52	78th Division.....	1,904	2.70
4th Division.....	2,472	3.50	79th Division.....	1,260	1.79
5th Division.....	1,418	2.01	80th Division.....	1,179	1.67
6th Division.....	103	.15	81st Division.....	208	.29
7th Division.....	910	1.29	82d Division.....	2,188	3.10
26th Division.....	5,793	8.21	83d Division.....	58	.08
27th Division.....	2,395	3.39	85th Division.....	1	.00
28th Division.....	4,631	6.56	88th Division.....	34	.05
29th Division.....	1,835	2.60	89th Division.....	1,974	2.80
30th Division.....	2,366	3.35	90th Division.....	2,218	3.14
32d Division.....	2,602	3.69	91st Division.....	598	.85
33d Division.....	2,854	4.05	92d Division.....	737	1.04
35th Division.....	1,729	2.45	Other arms.....	5,144	7.29
36th Division.....	577	.82	Not classified.....	3,240	4.59
37th Division.....	993	1.41			
41st Division.....	33	.05	Total.....	70,552	
42d Division.....	4,417	6.26			

¹ Compiled from data on file, Medical Division, Chemical Warfare Service.

² Exclusive of dead on battle fields and casualties of Marine Corps.

TABLE 2.—*Admissions for gas poisoning, by months of occurrence, American Expeditionary Forces. Absolute numbers and percentages of total number* ¹

Month	Number of admissions ²	Percent- age of total	Month	Number of admissions ²	Percent- age of total
February.....	95	0.13	September.....	9,948	14.10
March.....	535	.76	October.....	24,350	34.51
April.....	656	.93	November.....	3,667	5.20
May.....	2,638	3.74	Time not specified.....	461	.65
June.....	6,318	8.96			
July.....	9,945	14.10	Total.....	70,552	
August.....	11,939	16.92			

¹ Compiled from data on file, Medical Division, Chemical Warfare Service.

² Exclusive of dead on battle fields and casualties of Marine Corps.

^a Based on statistical tables, compiled in the Statistical Division of the Surgeon General's Office (on file, Historical Division, S. G. O.).

^b This number includes all cases of gas poisoning, even those for which a diagnosis tag was made on the field, the diagnosis of gassing not being confirmed later.

TABLE 3.—Admissions for gas poisoning, by gas, American Expeditionary Forces. Absolute numbers, deaths, and case mortality rates ¹

Gas to which exposed	Number of admissions ²	Deaths	Case mortality (per cent)
Gas, kind not stated.....	33,587	546	1.63
Chlorine.....	1,843	7	.38
Mustard.....	27,711	599	2.16
Phosgene.....	6,834	66	.97
Arsine.....	577	3	.52
Total.....	70,552	1,221	1.73

¹ From Report of the Surgeon General of the U. S. Army, 1920, p. 61.
² Exclusive of dead on battle fields and casualties of Marine Corps.

The records just quoted apply to officers and men of the Army who came under the care of the Medical Department. No record is available as to the number killed on the battle field by deleterious gases.

Gassing necessitated the discharge for disability of 2,853 officers and men. Discharges for disability for battle casualties totaled 20,588; gas, therefore, was responsible for 13.8 per cent of all discharges for disability for battle casualties.

The time lost in hospital during treatment for gas poisoning amounted to 2,947,199 days, or 16.8 per cent of all time lost in hospitals from battle injuries. The average amount of time lost for each patient admitted for gas poisoning was 41.77 days and for those who recovered 42.25 days. Of 69,301 gas patients whose injury did not prove fatal 33,253, or 47.13 per cent, were on sick report for less than 29 days, the average time lost for this class of cases being 13.45 days.

Table 4 gives the number of admissions by gas. The kind of gas was not specified in 47.61 per cent of all cases, chlorine was responsible for 2.61 per cent, mustard for 39.28 per cent, phosgene for 9.69 per cent, and arsine for 0.82 per cent. For the admissions in which the offending gas was definitely specified, 4.99 per cent due to chlorine, 74.96 per cent to mustard gas, 18.49 per cent to phosgene, and 1.56 per cent to arsine.

TABLE 4.—Admissions for poisoning by gas, officers and enlisted men, American Expeditionary Forces ¹

Gas to which exposed	Officers	Enlisted men			Total	Grand total
		White	Colored	Un-known		
Gas, kind not stated.....	1,249	24,290	526	7,522	32,338	33,587
Chlorine.....	31	1,607	36	169	1,812	1,843
Mustard gas.....	883	22,988	515	3,325	26,828	27,711
Phosgene.....	409	5,540	65	820	6,425	6,834
Arsine.....	31	345	117	84	546	577
Total.....	2,603	54,770	1,259	11,920	67,949	70,552

¹ From the Report of the Surgeon General of the U. S. Army, 1920, p. 58.

STATISTICAL ANALYSIS OF 546 AUTOPSY RECORDS OF GASED CASES

In order to obtain further information relative to the effects of the war gases, a detailed study was made of a series of autopsy protocols received in the office of the Division of Laboratories and Infectious Diseases, American Expeditionary Forces. This series consisted of 546 autopsy protocols of men who had

been exposed to the combat gases, although in all cases the gas was not responsible for death. While most of these fatalities were from the American forces, a few occurred in the Allied or German armies.

In analyzing this series of cases the clinical records and the reports of gas officers were frequently consulted for facts which were not obtainable from the protocols.

These autopsies were performed, in some instances, by medical officers trained to a certain extent in war-gas pathology, but, generally speaking, the records were filed by medical officers without a previous knowledge of the lesions to be expected from gas. Such records, therefore, give prominence only to the most notable gross lesions present. Since such lesions were usually those associated with the most striking phases of the clinical course, they are not without value. However, certain pathological changes due to gas poisoning are not apparent from these records.

An attempt to group the cases in the series definitely according to the gas or gases producing the lesions was found almost impossible; hence an arbitrary classification was employed. Gas groups are shown by the method adopted with a degree of accuracy sufficient for all practical purposes. The series is arranged in four groups:

A. Cases in which gas poisoning was apparently the principal immediate cause of death.

B. Cases in which the effect of gas poisoning was markedly augmented by subsequent infection with ordinary pyogenic organisms.

C. Cases of recent gas poisoning in which the principal immediate cause of death was gunshot wound or infectious disease.

D. Cases with a history of previous gas poisoning in which no apparent relationship existed between the poisoning and death.

Group A includes practically all cases in which death resulted from the effects of the suffocative gases (green cross substances—phosgene, diphosgene, chloropicrin, etc.), since deaths nearly always occurred with them before infections had had a chance to become established. Group B includes nearly all deaths due to mustard gas (yellow cross), or deaths resulting from a mixture of mustard gas with other gas used at the same time. Group C consists almost entirely of cases in which gas (usually mustard gas) played only a contributory rôle. Group D includes cases in which gas played no important part in the cause of death but in which there was a history of gassing at some previous date, and in which an effort was made to see what effect the former gassing had had on the tissues when subjected to a gross and microscopic examination. In addition, the relation of the gas poisoning to latent or active tuberculosis was studied.^c

Table 5 shows the various months in which exposure to gas occurred. By June, 1918, our troops had gained enough experience to make it difficult for the enemy to produce serious casualties by the use of green cross substances (phosgene, chloropicrin, etc.). Therefore, Group A now shows few cases. It should be stated, however, that during the rapid advance by our troops which occurred during the late months of the war it was difficult to get opportunities to examine Group A cases. They were comparatively few in number and some died soon after exposure and were disposed of on the battle field.

^c For pathological details see Chap. VI. The present discussion is intended merely to bring out some practical points in reference to deaths from gas poisoning.

TABLE 5.—Deaths from exposure to gas, by groups and by months of occurrence

Month	Groups				Total	Month	Groups				Total
	A	B	C	D			A	B	C	D	
March, 1918.....	0	4	0	1	5	October, 1918.....	9	189	36	25	259
April, 1918.....	0	0	0	0	0	November, 1918.....	0	10	0	2	12
May, 1918.....	19	4	1	0	24	December, 1918.....	0	0	0	0	0
June, 1918.....	0	19	2	1	22	January, 1919.....	0	0	0	0	0
July, 1918.....	1	31	9	0	41	February, 1919.....	1	0	0	0	0
August, 1918.....	1	71	13	5	90	Total.....	33	394	73	46	546
September, 1918.....	2	66	12	12	92						

Table 6 shows the type of gas to which the fatal cases coming to autopsy had been exposed, as shown by the clinical and gas officers' records.

There is no record of a case in this series of autopsies that was exposed to blue cross gas (ehlorarsine) alone.

TABLE 6.—Medical and gas officers' record of the type of gas to which the fatal cases coming to autopsy had been exposed

SECTION A. NUMBER OF CASES EXPOSED			
Type of gas to which exposed	Number of cases	Per-centage of total	
Yellow cross (mustard).....	245	44.87	
Green cross (suffocative type).....	31	5.68	
Blue, yellow, and green cross (simultaneous).....	94	17.22	
Yellow and green cross (simultaneous).....	41	7.51	
Blue and yellow cross (simultaneous).....	31	5.68	
Blue and green cross (simultaneous).....	3	0.55	
Yellow cross and green cross No. 1.....	1	0.18	
Blue cross, green cross, green cross No. 1, green cross No. 2, and green cross No. 3.....	1	0.18	
Unknown type or no record.....	98	17.95	
Total.....	546	100.00	

SECTION B. STUDY OF THE 447 CASES WITH KNOWN HISTORIES OF TYPE OF EXPOSURE IN THIS SERIES

Type of exposure	Number of cases	Percent- age of 447 cases
Yellow cross alone, and yellow cross with other gases.....	412	92.17
Green cross alone, and green cross with other gases.....	171	38.25
Blue cross with other gases.....	129	28.86

Table 7 gives, by groups, the gases believed to have been responsible for the lesions found. The list of casualties at home during the manufacture of war gas, the general casualty list from the battle field, hospital experience, and the findings in this series of autopsies, do not permit one to escape the conclusion that mustard gas (yellow cross) was preeminent in chemical warfare.

TABLE 7.—Series of fatal cases coming to autopsy by groups and by the gas believed to have been cause of lesions found

Type of gas	Group				Total of each gas	Per-centage of total cases
	A	B	C	D		
Yellow cross.....		373	67	23	463	84.80
Green cross.....	133	22	3	2	40	7.33
Yellow and green cross.....		12	1		13	2.38
No conclusion.....		7	2	21	30	5.49
Total in each group.....	33	394	73	46	546	
Percentage of total cases.....	6.04	72.16	13.37			100.00

¹ Phosgene, diposgene, chloropicrin, ethyldichlorarsine, and perhaps a rare instance of an extremely heavy concentration of mustard-gas vapor.

² Pneumonia a sequel.

Table 8 shows the character of the gas attacks to which these cases were subjected. Enemy projector attacks met with a certain amount of success in the early months of the American participation in the war, but later (against alert and well-trained troops) they produced comparatively small results. Near the close of the fighting a "rifled projector" was employed a few times,

but without noteworthy improvement in efficiency as compared with the old projector, except in its slightly increased range and the bare possibility of employing mustard-gas filling, which, up to that time, had never been used in such attacks.

TABLE 8.—*Character of gas attacks sustained*

Character of gas attacks unknown, but probably shell attacks	Number of cases	Percentage of total
Gas-shell attacks.....	402	73.63
Unknown but probably shell attacks.....	126	23.08
Projector attacks.....	18	3.30
Cloud wave attacks from cylinders.....	0	0.00
Total.....	546	

The duration of life after gassing is indicated in Table 9.

TABLE 9.—*Duration of life after gassing, by groups*

Group A			Group B			Group C			Group D		
Time, in days	Number of cases	Percentage of group	Time, in weeks	Number of cases	Percentage of group	Time, in weeks	Number of cases	Percentage of group	Time, in weeks	Number of cases	Percentage of group
1	19	57.58	1	146	37.06	1	5	6.85	1	3	6.52
2	7	21.21	2	149	37.82	2	7	9.59	2	3	6.52
3	4	12.12	3	49	12.44	3	10	13.69	3	4	8.70
4	1	3.03	4	25	6.36	4	6	8.22	4	3	6.52
5	2	6.06	5	11	2.79	5	7	9.59	5	4	8.70
			(?)	14	3.55	6-14	38	52.05	6-31	29	63.04
	33			394			73			46	

Group A.—These patients usually died within 24 to 48 hours, and sequelæ due to infection seldom occurred, contrary to the case in other kinds of gas poisoning.

Group B.—The majority of the fatalities in this group occurred between the close of the first week and the early part of the third week. Deaths were the result of infection which followed the gassing. Those dying later than the period mentioned usually developed one or more of the sequelæ common to any of the respiratory diseases.

Group C.—The duration of life after gassing was not closely related to the gas lesion found in the members of this group, since the gas was secondary in importance to some other disease or to some type of external violence such as gunshot wound which was immediately responsible for death.

Group D.—These deaths and the duration of life following the onset of the illness appear unrelated to gas unless it be admitted that in some instances a latent disease was fanned into activity by the exposure to gas.

Table 10 shows the causes of death. In certain cases under Group B in which there had been a light exposure to mustard gas, the respiratory lesions were very similar to those found in influenzal pneumonia. This disease was prevalent during the later part of the fighting period, and it is possible that some confusion existed in a few cases listed under Groups B and C.

TABLE 10.—*Causes of death*

Cause of death	Groups				Total	Cause of death	Groups				Total
	A	B	C	D			A	B	C	D	
Gas asphyxiation.....	27	6	0	0	33	Abscess of the lung.....	0	0	1	0	1
Tracheobronchitis and pneumonia.....	0	377	48	15	440	Anemia, primary.....	0	0	0	1	1
Empyema.....	0	1	1	1	3	Tuberculosis, acute miliary.....	0	0	0	2	2
Gangrene of the lungs.....	0	1	2	0	3	Tuberculosis of the lungs.....	0	0	0	5	5
Septicemia and pyemia.....	0	1	0	0	1	Embolism, pulmonary.....	0	0	0	1	1
No entry.....	0	8	1	1	10	Typhoid fever.....	0	0	0	1	1
Diphtheria.....	0	0	1	1	2	Abscess of the liver.....	0	0	0	1	1
Gunshot wounds.....	0	0	11	3	14	Infectious jaundice.....	0	0	0	1	1
Lobar pneumonia.....	6	0	4	4	14	Fracture, compound, of the skull.....	0	0	0	1	1
Cerebrospinal meningitis.....	0	0	2	5	7	Aneurysm.....	0	0	0	1	1
Pericarditis.....	0	0	1	1	2	Tuberculosis, disseminated.....	0	0	0	1	1
Simple forms of meningitis.....	0	0	1	0	1	Total.....	33	394	73	46	546

TABLE 13.—*Distribution of burns and pigmentation as described at autopsy, by region and by group*

Region	Group				Total	Region	Group				Total
	A	B	C	D			A	B	C	D	
Pelvic region:						Extremities:					
Genitals.....	1	210	9	3	223	Hands and arms.....	127	9	3		139
Buttocks.....		33	3	1	37	Feet and legs.....	52	2	1		55
Thighs.....		75	7		82	Total.....	179	11	4		194
Total.....	1	318	19	4	342	Trunk:					
Head and neck region:						Trunk (chest and abdomen).....	56	5	1		62
Face.....	1	198	7		206	Shoulders.....	59	3			62
Eyes.....		51		2	53	Axillæ.....	24	1			25
Neck.....		54	3	1	58	Total.....	139	9	1		149
Scalp.....		15	1		16	General:					
Total.....	1	318	11	3	333	Entire body.....	44		1		45
						Pigmentation.....	43	8	1		52

Table 14 indicates bacteriology, ante mortem and post mortem combined, of this series of cases.

TABLE 14.—*Bacteriology of cases studied*

	Sputum	Lung	Trachea	Bronchus	Throat	Pleura	Blood	Heart's blood	Sinus	Pericardium	Meninges	Spleen	Skin burn	Gunshot wound
GROUP B														
Pneumococcus (Type ?).....	6	31	0	1	0	2	0	5	0	0	0	0	0	0
Pneumococcus (Type I).....	0	2	0	0	0	0	0	4	0	0	0	0	0	0
Pneumococcus (Type II).....	1	1	0	0	0	0	0	0	0	0	0	0	0	0
Pneumococcus (Type III).....	1	1	0	0	0	0	1	0	0	0	0	0	0	0
Pneumococcus (Type IV).....	2	2	0	0	0	0	0	1	0	0	0	0	0	0
Streptococcus hæmolyticus.....	1	32	1	2	0	1	10	9	0	1	0	1	0	0
Streptococcus nonhæmolytic.....	1	29	2	0	0	1	0	0	0	0	0	0	0	0
Staphylococcus.....	1	7	0	1	0	0	0	1	0	0	0	0	0	0
B. influenza.....	3	15	5	0	0	0	0	0	0	0	0	0	0	0
B. diphtheriæ.....	0	0	0	1	5	0	0	0	1	0	0	0	0	0
Streptococcus viridans.....	1	1	0	0	0	0	0	0	0	0	0	0	0	0
Micrococcus catarrhalis.....	2	5	0	0	0	0	0	0	0	0	0	0	0	0
B. mucosus capsulatus.....	1	0	0	0	0	0	0	1	0	0	0	0	0	0
Meningococcus.....	0	2	1	0	0	0	0	0	0	0	0	0	0	0
Streptococcus mucosus.....	0	1	0	0	0	0	0	0	0	0	0	0	0	0
B. welchii.....	0	0	0	0	0	0	0	0	0	0	0	0	0	1
GROUP C														
Pneumococcus (Type ?).....	4	2	0	0	0	2	0	1	0	0	0	1	0	0
Pneumococcus (Type II).....	0	2	0	0	0	0	0	1	0	0	0	0	0	0
Pneumococcus (Type IV).....	1	0	0	0	0	0	1	3	0	0	0	0	0	0
Streptococcus hæmolyticus.....	0	8	1	0	0	4	0	8	0	0	0	0	0	0
Streptococcus nonhæmolytic.....	1	3	0	0	0	0	0	1	0	0	0	0	0	0
Staphylococcus.....	0	2	0	0	0	0	0	1	0	0	0	0	0	0
B. influenza.....	0	7	0	0	0	0	0	0	0	0	0	0	0	0
B. diphtheriæ.....	0	0	0	0	0	3	0	0	0	0	0	0	0	0
Streptococcus viridans.....	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Meningococcus.....	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Micrococcus catarrhalis.....	0	1	0	0	0	0	0	0	0	0	0	0	0	0
B. welchii.....	0	0	0	0	0	0	0	0	0	0	0	0	0	1
GROUP D														
Pneumococcus (Type ?).....	0	4	0	0	0	0	0	3	0	0	1	0	0	0
Pneumococcus (Type II).....	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Pneumococcus (Type IV).....	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Streptococcus hæmolyticus.....	2	1	0	0	0	2	0	1	0	0	0	1	0	0
Streptococcus nonhæmolytic.....	0	6	0	0	0	0	0	0	0	0	0	0	0	0
Staphylococcus.....	0	0	0	0	0	0	0	1	0	0	0	0	0	0
B. influenza.....	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Tubercle bacillus.....	5	3	0	0	0	0	0	0	0	0	0	0	0	0
Meningococcus.....	0	0	0	0	0	0	0	0	0	0	3	0	0	0

Table 15 clearly shows the similarity of the organisms recovered in cultures from these cases with those from the usual respiratory diseases studied at autopsy. There is the same predominance of the streptococcus and pneumococcus.

TABLE 15.—*Organisms isolated in the series of cases*

Organisms	Sputum	Lung	Trachea	Bronchus	Throat	Pleura	Blood	Heart's blood	Sinus	Pericardium	Meninges	Spleen	Skin burn	Gunshot wound	Total
Streptococcus.....	6	82	4	2	-----	8	10	19	-----	1	-----	2	-----	-----	134
Pneumococcus.....	16	46	-----	1	-----	4	2	18	-----	-----	1	1	-----	-----	89
B. influenzae.....	3	23	5	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	31
Staphylococcus.....	1	9	-----	1	-----	-----	-----	3	-----	-----	-----	-----	1	-----	15
B. diphtheriae.....	-----	-----	-----	-----	5	3	-----	-----	1	-----	-----	-----	-----	-----	10
B. tuberculosis.....	5	3	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	8
M. catarrhalis.....	2	6	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	8
Meningococcus.....	-----	2	1	-----	-----	-----	-----	-----	-----	-----	4	-----	-----	-----	7
B. welchii.....	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	2	2
B. mucosus capsulatus.	1	-----	-----	-----	-----	-----	-----	1	-----	-----	-----	-----	-----	-----	2

AFTER-EFFECTS OF GAS POISONING

A study was made of 3,014 casualties caused by poisonous gases in the American Expeditionary Forces during the World War. It appears from the Annual Report of the Surgeon General for 1920 that the total number of casualties from gas poisoning was 70,552, of which 1,843 were caused by chlorine, 6,834 by phosgene, 27,711 by mustard gas, and the remainder (33,587) by various unidentified gases. The original contemplation was to base this study on 1,000 cases each of chlorine, phosgene, and mustard-gas casualties, the three most important gases employed in the war; but of the 1,843 casualties from chlorine gas reported, sufficiently complete records of only 838 cases could be found. However, to bring up the series to the contemplated 3,000 (3,014), records of 160 casualties caused by either unknown, mixed, or two different gases at different dates are included.

The physical and mental status of each of these cases at the termination of treatment in Army hospitals, or at the time of final separation from the service having been determined, this status was then followed, through the courtesy and cooperation of the United States Veterans' Bureau, up to the present time (January to August, inclusive, 1924, this being the period in which reports were obtained from the Veterans' Bureau). Complete tables were compiled for each gas and for the mixed gases; the results are summarized in Table 16.

It is believed that the results thus presented are reasonably accurate, though necessarily they are not absolute by reason of difficulties encountered, in some instances, in the interpretation, sometimes arbitrary, of illegible, ambiguous, or contradictory records, many of which were probably written under stress of fire. In some instances an associated injury existed or an extraneous complication developed, prolonging hospitalization, the entire period of which, consequently, should not be charged to gas. The term "gassed" or "effects of gas," without qualifying expression, appeared frequently; it is probable that in the haste and confusion of demobilization some disabilities (usually small percentages—5 or 10 per cent) from the effects of gas were noted on discharge papers, possibly on the mere strength of the soldier's statement that he had been "gassed," and after only a very cursory routine examination.

It was originally necessary, and for a while was the established policy in the Veterans' Bureau, to award compensation to claimants upon certification by any physician, not in the bureau employ, pending subsequent careful examination by a bureau physician. For this reason the value of the results in the tables presented indicating the number awarded compensation, which was subsequently discontinued, is depreciated; although by far the greater number of these discontinuances were in all probability due to recoveries, or at least to improvements to degrees less than 10 per cent (the minimum for which compensation is allowed) from actual impairments. This should not apply, however, to other results shown; for instance, to those at present under compensation, inasmuch as, with the development of the Veterans' Bureau, examinations were standardized and made at periodic intervals.

For a clear comprehension of the subjoined table, it is necessary for the reader to understand that the Veterans' Bureau which, by legislative enactment,¹ culminated from the original Bureau of War Risk Insurance, provides for disabled veterans of the World War by means of a system of hospitalization, when indicated; by monetary compensation based on a standard of \$80 per month for total incapacity (100 per cent), varying by degrees to the minimum (10 per cent) incapacity for which compensation is allowed; or by vocational training, which included also a monetary allowance, in various professions, crafts, and trades. Vocational training is allowed, when desired, to claimants with disabilities of less than 10 per cent, who are ineligible, therefore, for compensation. Many claimants under compensation alternate periods of compensation with periods of vocational training, and for these reasons the terms "compensation" and "vocational training" are employed synonymously for the purpose of this study. However, in this presentation there are only eight instances of vocational training following disallowance of compensation. In the many cases in which the compensatory status exacerbated during the compensation period, the figures representing the degree of compensation indicate the percentage last awarded. It should be borne in mind that the entry, "no claim made," has reference here solely to disability from gassing. In some instances the Veterans' Bureau records show that compensation is being paid, but for some condition for which the gassing was in nowise responsible.

In the prosecution of this study four tables were prepared, three relating, respectively, to chlorine, phosgene, and mustard gas casualties, the fourth to various mixed gases, and gases, variety unknown (on file, Historical Division, Surgeon General's Office).

SUMMARY OF TABLE OF 838 CHLORINE GAS CASUALTIES

The average period of treatment in hospital of the casualties from chlorine gas is shown to be 53.5 days. Of the 838 casualties from chlorine gas considered, the deaths of 28 are recorded, 16 of these having been caused by traumatism other than gassing, and 12 by disease, 19 occurring in service and 9 after discharge from service. Of the 12 caused by disease, 6 occurred in service and 6 after discharge from service. Of the 6 occurring in service, 1 died of bronchopneumonia 5 days after exposure; 1 of bronchopneumonia 9 days after date of gassing; 1 of bronchopneumonia 193 days after date of gassing (readmitted to hospital after original admission and returned to duty—may or may not have

been due to gas): 1 of lobar pneumonia 57 days after date of gassing; 1 of purulent pleurisy 92 days after date of gassing (readmitted to hospital for after-effects of gas after original admission and return to duty); and 1 of tuberculous meningitis 229 days after date of gassing. Of the 6 deaths from disease occurring after discharge from service, the records do not indicate gas as a causative factor, with the possible exception of 1 from pulmonary tuberculosis which occurred 962 days after date of gassing, after having received 100 per cent compensation, which began 830 days after date of gassing. It therefore appears that 2 deaths are directly attributable to gas; 3 of the others possibly depending on gas as the causative factor. Only one death among those separated from the service on surgeon's certificate of disability or awarded a disability rating upon demobilization is recorded; this was by suicide $3\frac{1}{2}$ years after date of gassing, the patient having been discharged on surgeon's certificate of disability for psychoneurosis, neurasthenia, effort syndrome, and myocarditis, the cause of which is not determinable from the records.

Twenty were discharged on surgeon's certificate of disability—9 for disabilities directly attributed to gas, 1 for disability in part caused by gas, 6 for disabilities not caused by gas, and 4 for disabilities the causes of which are indeterminable from the records. Of the 9 cases attributed to gas, the average disability was 31.4 per cent and the average period between date of gassing and date of discharge was 298 days. The disabilities were: Pulmonary tuberculosis, 2; bronchitis, 2; pleurisy, 1; neurocirculatory asthenia, 1; heart (tachycardia, dyspnea, and neurocirculatory asthenia), 1; "effects of gas," 1; and nephritis, 1. Of these 9 cases the records show that 7 are now under compensation, the compensable disability in some instances not being identical with the disability for which discharged; 1, discharged for pulmonary tuberculosis, inactive, made no claim, and 1, discharged for nephritis, made claim which was disallowed. The case attributed in part to the effects of gas was discharged by reason of gunshot wound of right shoulder, as the major disability, with tracheitis due to gas as a secondary condition; disability 25 per cent; discharged 438 days after date of gassing. This case is now under compensation, 25 per cent, for disease of upper respiratory tract. Of the 4 disabilities the causes of which are indeterminable from the records, 1 was discharged 310 days after date of gassing, 10 per cent disability, for tuberculous epididymitis and pulmonary tuberculosis, chronic, inactive, and is now receiving 100 per cent compensation for pulmonary tuberculosis, chronic, and tuberculous epididymitis; 1 was discharged 423 days after date of gassing, disability, 10 per cent for neurasthenia, effort syndrome, and myocarditis, and received 100 per cent compensation for psychosis until terminated by death; 1 was discharged 345 days after date of gassing, disability, 30 per cent, for bronchitis and neurocirculatory asthenia, and is now receiving 10 per cent compensation for pulmonary tuberculosis; and the fourth was discharged 390 days after date gassed, disability, 30 per cent, for otitis media, bilateral, and is now receiving compensation, 32 per cent, for pulmonary tuberculosis and otitis media, bilateral.

The records show that 49 cases were rated a disability at time of discharge from service, 39 being directly attributable to gas, 9 to other causes, and 1 cause indeterminate. Of the 39 cases attributed to gas, the average disability rating was 11.15 per cent and the causes recorded were bronchitis, 24;

pleurisy, 1; laryngitis, 1; valvular heart disease, 2; eyes (1 keratitis, 1 conjunctivitis), 2; and "after effects of gas," 9. The average disability of the 24 discharged with bronchitis was 12.5 per cent and the average interval between date of gassing and date of discharge was approximately 240 days. The 1 indeterminate case is recorded as discharged with a disability of 25 per cent for defective vision, right, the cause not being given. Of the 39 cases attributed to gas, 19 are now receiving compensation, in most instances for the same condition noted upon demobilization as the disabling factor. Of the remaining 20, 6 have made no claim for compensation, 4 claims made have been disallowed, and compensations, after having been awarded and paid, for varying periods, to 10, have been discontinued.

Of this series of 838 cases, 19 died in service, and the records of the United States Veterans' Bureau show that 360 cases have made no claim for compensation, 179 claims have been disallowed, 3 claims are pending action, 86 compensations were awarded and subsequently discontinued after varying periods, and 191 are now under compensation or vocational training. Of the 86 discontinued compensations, 5 were for pulmonary tuberculosis, 44 bronchitis, 13 heart abnormalities, 2 upper respiratory tract conditions, 9 "gassed," and 13 all others. The average compensation period of the 5 tuberculosis cases was 986 days and of the 44 bronchitis cases 1,073 days. Only one of the five compensations for pulmonary tuberculosis was discontinued by death.

Of the 191 cases under compensation or vocational training the compensable disabilities recorded are: Pulmonary tuberculosis, 60; bronchitis, 68; disease of the upper respiratory tract, 6; disease of heart, 21; disease of eyes, 7; disease of nervous system, 17; "gassed," 4; all others, 8. Of the 60 tuberculosis cases, the average disability is 53 per cent and the average period between the date of gassing and beginning of compensation is 379.5 days. Of the 68 cases of bronchitis the average disability is 20.46 per cent, and the average period between the date of gassing and beginning of compensation is 357.8 days. Of the total number under compensation, 32 are receiving the maximum rate of 100 per cent and 67 are receiving the minimum rate of 10 per cent.

SUMMARY OF TABLE OF 1,000 PHOSGENE GAS CASUALTIES

The average period of hospitalization of the casualties from phosgene gas is shown to be 44.7 days. Of the 1,000 casualties from this gas considered, the deaths of 37 are recorded, 26 of which occurred in service and 11 after discharge from service; 17 were caused by traumatism other than gassing, and 20 by disease. Of the 20 caused by disease, 11 occurred in service and 9 after discharge from service. Of the 11 occurring in service, 1 died within 24 hours and 1 within 48 hours from the effects of phosgene gas; 1 within 6 days, of which no symptoms are recorded; 4, of bronchopneumonia, 25, 36, 40, and 200 days, respectively, from date of gassing (these 4 cases were originally returned to duty 2, 3, 6, and 22 days, respectively, from date of gassing, and were readmitted to hospital only a few days prior to death); 2, of lobar pneumonia, 125 and 144 days, respectively, from date of gassing, 1 of which was originally in hospital for only 26 days, dying the day following readmission, no details being recorded, other than that there was a complication of diphtheria mentioned in connection with the death of the other; 1 of pulmonary abscess, 130 days after date of gassing, originally in hospital only 3 days, and

died 10 days after readmission; and 1 of tuberculous meningitis, 240 days after date of gassing. Of the 11 deaths occurring after discharge from service, 2 were caused by traumatism and 9 by disease. Of the 9 caused by disease, 5 were from pulmonary tuberculosis, occurring from 18 to 54 months after date of exposure to gas, all of which were under 100 per cent compensation for tuberculosis, and gas may or may not have been a factor in the death. Of these 1 was in hospital for only 10 days from date of gassing, compensation beginning 309 days after date of gassing; 1 was in hospital for 45 days from date of gassing for bronchitis, compensation beginning 292 days after date of gassing. The other three were in hospital for 16, 72, and 53 days, respectively, from date of gassing and were awarded compensation 115, 934, and 223 days, respectively, from date of exposure to gas. Gas is not indicated as a causative factor in the deaths of the remaining 4 occurring after demobilization. It therefore appears that only 3 deaths can be directly attributed to gas, gas being a possible factor, which can not be definitely determined from the records, in the deaths of several others. No death among those separated from service on surgeon's certificate of disability or awarded a disability rating upon demobilization is recorded.

Of these 1,000 cases, 10 were discharged on surgeon's certificate of disability, 4 for disabilities directly attributed to gas, 1 for disability in part caused by gas, and 5 for disabilities not caused by gas. Of the 4 cases attributed to gas the average disability was 33.75 per cent, and the average period between the date of gassing and the date of discharge, 219 days; the disabilities were, bronchitis, 3, and valvular heart disease, mitral insufficiency, 1. The records show that these 4 cases are now under compensation for the conditions for which discharged. The case attributed in part to the effects of gas was discharged for bronchitis and dyspnea on exertion, 186 days after date of gassing, with a history of pneumonia in 1902 and in 1909. This case is now receiving 10 per cent compensation for bronchitis and tuberculosis.

The records show that 54 cases were rated a disability at time of discharge from service, of 41 cases being attributed to gas, 1 partly due to gas, and 12 to causes other than gas. Of the 41 cases attributed to gas the average disability rating was 9.39 per cent and the causes recorded were pulmonary tuberculosis, 3; bronchitis, 31; disease of upper respiratory tract, 1; disease of heart, 3; "after effects of gas," 2, and dyspnea, 1. The average disability of the 3 discharged with tuberculosis was 11.66 per cent, and the average interval between the date of exposure and the date discharged was 167 days. The average disability of the 31 discharged with bronchitis was 9.2 per cent and the average interval between the date of gassing and date discharged was 237 days. The one case with disability partly due to gas is recorded as having been discharged with a disability of 10 per cent, 138 days after date gassed, for goitre (existed prior to enlistment), and "history of gas." Of the 41 cases attributed to gas, 22 are now receiving compensation, in most instances for the same disability recorded upon demobilization as the disabling factor. Of the remaining 19, 4 have made no claim for compensation, 4 claims have been disallowed, 1 claim is pending action, and compensations, after having been awarded and paid for varying periods to 10, have been discontinued. The 3 cases with the disability rating for tuberculosis upon discharge have all been compensated for tuberculosis, 2 now remaining under compensation, and the third having been discontinued after a compensation period of 1.569 days.

Of this series of 1,000 cases, 26 died in service and the records of the United States Veterans' Bureau show that 446 have made no claim for compensation, 212 claims have been disallowed, 4 claims are pending action, 112 compensations awarded have been discontinued after varying periods, and 200 are now under compensation or vocational training. Of the 112 discontinued compensations, 9 were for pulmonary tuberculosis, 63 for bronchitis, 8 for heart abnormalities, 4 for upper respiratory tract conditions, 9 for "gassed," and 19, all others. The average compensation period of the 9 tuberculosis cases was 905 days and of the 53 bronchitis cases, 1,150 days. Five of the compensations for tuberculosis discontinued were terminated by death. Of the 200 cases under compensation or vocational training, the compensable disabilities recorded are: Pulmonary tuberculosis, 42; bronchitis, 91; disease of the upper respiratory tract, 9; disease of the heart, 16; disease of eyes, 3; disease of nervous system, 20; disease of kidneys, 2; "gassed," 6; all others 11. Of the 42 tuberculosis cases, the average disability is 56.6 per cent, and the average period between the date of gassing and beginning of compensation is 421 days. Of the 91 cases of bronchitis, the average disability is 26.2 per cent, and the average period between the date of gassing and beginning of compensation is 328.7 days. Of the total number under compensation, 33 are receiving the maximum rate of 100 per cent and 77 the minimum rate of 10 per cent.

SUMMARY OF TABLE OF 1,016 MUSTARD GAS CASUALTIES

The average period of treatment in hospital of the casualties from mustard gas is shown to be 62.55 days.

Of the 1,016 casualties from mustard gas considered, the deaths of 63 are recorded, 40 of which occurred in service and 23 after discharge from service, 17 having been caused by traumatism other than gassing and 46 by disease. Of the 46 caused by disease, 26 occurred in service and 20 after discharge from service. Of the 26 occurring in service, 7 resulted from bronchopneumonia or other immediate effects of gas within 7 days from date of gassing; 14 occurred within 30 days, from bronchopneumonia or other immediate effects of gas, including a pseudomembranous laryngitis in one instance, various burns, with accompanying edema and toxemia, in three instances, and a tracheitis or a tracheobronchitis in a number of instances; 1 occurred 62 days after date of gassing, from lobar pneumonia (originally in hospital 51 days, death 2 days subsequent to readmission); 1 occurred 61 days after date of gassing, from bronchopneumonia, ulcerated larynx, and pulmonary tuberculosis; 1 occurred 157 days after date of gassing, from lobar pneumonia (originally in hospital 63 days, and died 7 days subsequent to readmission); 1 occurred 197 days after date of gassing, from bronchopneumonia, pneumothorax, and empyema; and 1 occurred 14 days after date of gassing, from cerebrospinal meningitis, which developed 2 days prior to death and which bore no relationship to gas. Of the 14 cases which died within 30 days from date of exposure to gas, 10 sustained minor gunshot wounds, associated with the gassing, but the records do not indicate that these injuries operated as a factor in the cause of death, with the possible exception of 1 case which died, 10 days after date of gassing, from bronchopneumonia, and which developed a *B. welchii* infection of a gunshot wound of the ankle.

Of the 23 deaths occurring after discharge from service, 3 were caused by traumatism and 20 by disease. Of the 20 caused by disease, 11 were due to pulmonary tuberculosis, occurring from 587 to 1,995 days after date of gassing. Of these 11, 8 were receiving 100 per cent compensation for tuberculosis, gas origin being indicated in the case of 2, and the records, in the case of the other 6, showing that 1 was in hospital only 4 days, no symptoms recorded, and received compensation 967 days after date when gassed; 1 was in hospital 6 days, no symptoms recorded, and received compensation 866 days after date when gassed; 1 was in hospital 40 days, slight bronchial symptoms, and received compensation 249 days after date when gassed; 1 was in hospital 33 days, symptoms pharyngitis and bronchial soreness, and received compensation 169 days after date when gassed; 1 was in hospital 42 days, symptoms bronchitis, and received compensation 172 days after date when gassed; and 1 was in hospital 58 days, symptoms conjunctivitis, and received compensation 1,174 days after date when gassed; 1 was receiving 100 per cent compensation for adhesions subsequent to pneumonia, which followed gassing, and 2 made no claim for compensation (the records show definitely that 1 of these was not of gas origin). Two died of pneumonia, 833 and 1,154 days, respectively, after exposure to gas, the one being under 10 per cent compensation for pharyngitis and conjunctivitis, and the other under 20 per cent compensation for atrophy of optic nerve and cardiac hypertrophy. Gas is not indicated as a causative factor in the death of the remaining 7, occurring from disease, after demobilization. It appears, therefore, that 24 deaths were directly attributed to gas and that gas was a possible factor in the deaths from pneumonia and from tuberculosis of a number of others, the primary cause of which can not be determined from the records. Of the 11 deaths from pulmonary tuberculosis, after discharge from service, 3 had been discharged on surgeon's certificate of disability (2 for pulmonary tuberculosis and the third for adhesions from pneumonia, following gas). Of the other 9 deaths from disease after discharge from service, only 1 had been discharged on surgeon's certificate of disability (for mental deficiency, moron), and he died, 1,842 days after date of gassing, from valvular heart disease. Of the deaths from disease, after discharge from service, only 1 had been awarded a disability rating upon demobilization, for atrophy of right testicle, existing prior to enlistment, and bronchitis, 35 per cent disability, 103 days after date of gassing. This case was under 10 per cent compensation for bronchitis and pulmonary tuberculosis, and was terminated by death from encephalitis, 862 days after exposure to gas.

Of the cases of this group 27 were discharged on surgeon's certificate of disability, 12 for disability directly attributed to gas, 4 for disability in part caused by gas, 10 for disability not caused by gas, and 1 for disability, cause indeterminable from the records. Of the 12 cases attributed to gas, the average disability was 21.9 per cent and the average period between date of gassing and date of discharge, 274 days; the disabilities were: Pulmonary tuberculosis, 2; pleurisy, 1; bronchitis, 6; nervous system, 2; and corneal opacity, 1. The records show that: The 2 discharged for pulmonary tuberculosis died from pulmonary tuberculosis (one, 1,137 and the other 1,955 days after date gassed); 1 discharged for pleurisy died from tuberculosis 587 days after date gassed; of the 6 discharged for bronchitis, 1 was disallowed compensation, 3 claims for bronchitis were awarded and the compensation subsequently discontinued.

1 is receiving compensation for bronchitis, and 1 is receiving compensation for a heart condition; of the 2 discharged for conditions of the nervous system, 1 made no claim and the other is receiving compensation for practically the same condition for which discharged; 1, discharged for corneal opacity, is being compensated for the same condition. Of the 4 with disability attributed in part to gas, 1 was discharged, 50 per cent disability, for a preexisting retinochoroiditis, aggravated by gas, 241 days after exposure to gas, and was awarded 30 per cent compensation for same 241 days after date gassed, which was subsequently discontinued; 1 was discharged, 50 per cent disability, for endocarditis, mitral incompetency (line of duty), and mental deficiency, moron (existed prior to enlistment), 239 days after date of gassing and is receiving 75 per cent compensation for valvular heart and hypomania; 1 was discharged with 35 per cent disability, for bronchitis, adhesions following appendectomy, flat-foot, tachycardia, and dyspnea, 282 days after date of gassing, and is receiving 20 per cent compensation for bronchitis; and 1 was discharged with 40 per cent disability for dyspnea, cough, prolonged expiration and goiter, 316 days after date gassed, and is receiving 10 per cent compensation for "gassed." The case for which the cause of discharge is indeterminable from the records was originally in hospital 28 days, readmitted 150 days later with pain in side, had a history of measles 11 months before first admission, was discharged, 50 per cent disability, for pleuritic adhesions, 422 days after exposure to gas, and is receiving 50 per cent compensation for pulmonary tuberculosis.

The records show that 57 cases were rated a disability at time of discharge from service, 33 cases being attributed to gas, 6 partly due to gas, 15 to causes other than gas, and 3 to causes indeterminable from the records. Of the 33 cases attributed to gas, the average disability rating was 11.36 per cent and the causes recorded are: Bronchitis, 24; pleurisy, 1; functional disorder of heart, 1; eyes, 2 (1 defective vision and 1 conjunctivitis); "history of gassing," 1; dyspnea, 1; and "after effects" of gas burns, 3. The average disability of the 24 discharged with bronchitis was 12.29 per cent, and the average interval between date of gassing and date of discharge was 207 days. Of the 33 cases attributed to gas, 17 are now receiving compensation, in most instances for the same disability recorded under demobilization as the disabling factor; 7 were awarded compensations which were subsequently discontinued; 5 made no claim, and claims of 4 were disallowed. Of the 6 cases with disabilities partly due to gas, 1 was discharged with 15 per cent disability for bronchitis and flat-foot, 1 with 35 per cent disability for bronchitis and atrophy of right testicle; 1 with 10 per cent disability for bronchitis and flat-foot; 1 with 25 per cent disability for tuberculosis (existed prior to enlistment), aggravated by gassing; 1 with 5 per cent disability for bronchitis and gunshot wound of left ankle, and 1 with 10 per cent disability for gunshot wound of finger, neurasthenia, and "gassed." Of the 3 cases discharged with disabilities the causes for which are indeterminable from the records, 1 was discharged, disability, 10 per cent, 226 days after date of gassing, for thickened pleura, following bronchopneumonia, which developed 136 days after an original stay in hospital of only 17 days, and is now receiving 10 per cent compensation for pulmonary tuberculosis; 1 was discharged, disability, 10 per cent, 228 days after date of gassing, for "harsh, high-pitched breathing," after an original stay in hospital

of 63 days, during which no symptoms are recorded, and is receiving 25 per cent compensation for pulmonary tuberculosis; and 1 was discharged, disability, 10 per cent, 173 days after date of gassing, for "harsh, high-pitched breathing," after an original stay in hospital of 29 days, with readmission period of 30 days, for lobar pneumonia, and whose claim for compensation was disallowed.

Of this series of 1,016 cases, 40 died in service; the records of the United States Veterans' Bureau show that 467 have made no claim for compensation; 194 claims have been disallowed; 6 claims are pending action; 117 compensations awarded have been discontinued after varying periods; and 192 are now under compensation or vocational training. Of the 117 discontinued compensations, 20 were for pulmonary tuberculosis, 66 for bronchitis, 8 for heart abnormalities, 1 for pharyngitis, 9 for "gassed," and 13 all others. The average compensation period of the 20 tuberculosis cases was 998 days and of the 66 bronchitis cases 1,179 days. Nine of the discontinued compensations for tuberculosis were terminated by death. Of the 192 cases under compensation or vocational training, the compensable disabilities recorded are: Pulmonary tuberculosis, 63; bronchitis, 79; laryngitis, 1; disease of heart, 10; disease of eyes, 6; disease of nervous system, 15; "gassed," 7; all others, 11. Of the 63 tuberculosis cases the average disability is 41.5 per cent and the average period between date gassed and beginning of compensation is 397 days. Of the 79 cases of bronchitis, the average disability is 29.34 per cent, and the average period between date of gassing and the beginning of compensation is 301 days. Of the total number under compensation, 24 are receiving the maximum rate of 100 per cent and 67 the minimum rate of 10 per cent.

SUMMARY OF TABLE OF 160 CASUALTIES FROM MIXED GASES, AND GASES, VARIETY UNKNOWN

The average period of hospitalization of the total casualties from gases recorded and classified in this study as mixed is shown to be 67 days. Of the 160 casualties from mixed gases considered, the deaths of 4 are recorded, 3 of which occurred in service and 1 after discharge from service; 3 were caused by traumatism and 1 by disease. The death caused by disease occurred in service from bronchopneumonia, 13 days after date of gassing; therefore only 1 death in this series is attributed to gas. No death is recorded among those discharged on surgeon's certificate of disability or with disability on demobilization.

Five were discharged on surgeon's certificate of disability, 3 for disabilities directly attributed to gas, 1 for disability not due to gas, and 1 for disability, cause indeterminable from the records. Of the 3 cases attributed to gas, the average disability on discharge was 28.3 per cent and the average period between date of gassing and date of discharge was 350 days. The disabilities were: Pulmonary tuberculosis, 1; disability, 35 per cent, discharged 429 days after date of gassing, now receiving 100 per cent compensation for tuberculosis; 1 for dyspnea, cough and effort syndrome, disability, 50 per cent, discharged 252 days after date of gassing, awarded compensation for bronchitis, since discontinued; and 1 for myocarditis, cardiac hypertrophy, and dilatation, disability, 20 per cent, discharged 369 days after date of gassing, now receiving 10 per cent compensation for mitral insufficiency. The case for which the cause for discharge is indeterminable was discharged, disability, 50 per cent, 273 days after date of gassing for cardiac hypertrophy, dyspnea, and tachycardia, after

an original stay in hospital of 92 days for bronchitis, with a readmission 90 days later for effort syndrome, and is now receiving 25 per cent compensation for bronchitis.

Twelve cases were rated a disability at time of discharge from service. Of these, 10 were attributed to gas and 2 to causes other than gas. Of the 10 attributed to gas, the average disability rating was 12.3 per cent and the causes recorded were: Pulmonary tuberculosis, 1, disability 33 $\frac{1}{4}$ per cent; bronchitis, 7; "disordered heart," 1; and "nervousness," 1. The average disability of the 7 discharged with bronchitis was 10 per cent and the average interval between date of gassing and date of discharge was 247 days. Of the 10 cases attributed to gas, 4 are now receiving compensation (2, including the case discharged with pulmonary tuberculosis, for the same disability existing upon discharge; the 1 discharged with "disordered heart," for pharyngitis; and the 1 discharged with "nervousness," for pulmonary tuberculosis); 3 were awarded compensations which were subsequently discontinued; and 3 made no claim for compensation.

Of this series, totaling 160 cases, 3 died in service, and the records of the United States Veterans' Bureau show that 60 have made no claim for compensation. Thirty-four claims have been disallowed, 24 compensations were awarded and discontinued after varying periods, and 39 are now under compensation or vocational training. Of the 24 discontinued compensations, 2 were for pulmonary tuberculosis, 16 for bronchitis, 1 for "throat and tonsils," 2 for "gassed," and 3, all others. The average compensation period of the 2 tuberculosis cases was 1,206 days and of the 16 bronchitis cases, 1,283 days. None of the discontinued compensations were terminated by death. Of the 39 under compensation or vocational training, the compensable disabilities recorded are: Pulmonary tuberculosis, 9; bronchitis, 15; pharyngitis, 1; disease of heart, 8; disease of eyes, 1; "gassed," 2; all others, 3. Of the 9 tuberculosis cases, the average disability is 49.4 per cent and the average period between date of gassing and beginning of compensation 395 days. Of the 15 bronchitis cases the average disability is 20 per cent and the average period between date of gassing and beginning of compensation 287 days. Of the total number under compensation, 3 are receiving the maximum rate of 100 per cent and 14 the minimum rate of 10 per cent.

SUMMARY OF STUDY OF 3,014 GAS CASUALTIES

Table 16 consists of a résumé of the four tables summarized in the preceding text.

The average period of hospitalization of the entire 3,014 gas casualties was found to be 54.34 days. The hospitalization period appears to have been greater for the mustard gas than for either the chlorine or phosgene gas casualties, the probable explanation being that surface burns in many instances prolonged hospitalization.

Of the 79 deaths from disease, 30 (0.99 per cent of total cases, 22.72 per cent of total deaths and 37.97 per cent of total deaths from disease) were obviously due to the effects of gas, 12 dying within 10 days, 15 within 30 days, 1 in 61 days, 1 in 1,137 days, and 1 in 1,955 days. All but the last 2 of these died in service and 24 of the 30 died from the effects of mustard gas. Of the 44

TABLE 16.—A study of 3,014 gassed cases, American Expeditionary Forces (1917-18) with a view to determine after-effects. Numbers and percentage of the total number of cases of the series and of certain specific classes for each result. Average percentage of disability in specific classes^{1,2}

[Numbers in italic are not included in totals]

	Chlorine			Phosgene			Mustard			Mixed			Total		
	838 cases		Per-centage of each specific disability class	1,000 cases		Per-centage of each specific disability class	1,016 cases		Per-centage of each specific disability class	160 cases		Per-centage of each specific disability class	3,014 cases		Per-centage of each specific disability class
	Num-ber	Per-centage		Num-ber	Per-centage		Num-ber	Per-centage		Num-ber	Per-centage		Num-ber	Per-centage	
Deaths:															
From traumatism—in service	13	1.55		15	1.50		14	1.37		2	1.25		44	1.46	
From traumatism after demobilization	3	.36		2	.20		3	.29		1	.62		9	.29	
From disease, in service	6	.71		11	1.10		26	2.55		1	.62		44	1.46	
From disease after demobilization	6	.71		9	.90		20	1.96		1	.62		35	1.16	
Total	28	3.34		37	3.70		63	6.20		4	2.50		132	4.37	
Obviously from effects of gas	2	.24		3	.30		24	2.36		1	.62		30	.99	
Obviously not from the effects of gas	23	2.74		25	2.50		39	2.95		3	1.87		81	2.68	
Cause indeterminate (as regards gas as a causative factor)	3	.36		9	.90		9	.88							
From pulmonary tuberculosis	1	.12		5	.50		11	1.08					21	.69	
From pneumonia (in service only)	4	.48		9	.90		15	1.47		1	.62		17	.56	
													29	.96	
Discharges on surgeon's certificate of disability:															
For conditions resulting from effects of gas	9	1.07	31.38	4	.40	33.75	12	1.18	30.20	44.44	3	1.87	28.33	60	2.02
For conditions not resulting from effects of gas	6	.71	30	5	.50	50	10	.98	37.03	1	.62		22	.73	
For conditions in part resulting from effects of gas	1	.12	5	1	.10	10	4	.39	14.81				6	.19	
For conditions, gas as a causative factor indeterminate	4	.48	20				1	.09	3.70	1	.62	20	6	.19	
Total	20	2.38	25.87	10	1	36.50	27	2.65	37.54	5	3.12	42	62	2.05	33.97
Resulting from effects of gas—															
For pulmonary tuberculosis	2	.24	18.75				2	.19	87.50	16.62	1	.62	35	33.33	17.85
For bronchitis	2	.24	40	3	.30	25	6	.59	20.41	50	1	.62	30	33.33	42.85
For disease of eyes	1	.12		1	.10		1	.09	8.33	8.33	1	.62	3	.09	3.57
For all other diseases	4	.48	44.44				3	.29	25	25			7	.23	10.71
Since died							3	.29	25	25			7	.23	10.71
Under compensation	7	.83	54.57	4	.40	36.25	4	.39	16.25	33.33	2	1.25	55	66.66	60.71
Average period (days) from date gassed	298			219			274				350		17		
Claims for compensation not made	1	.12	11.11				1	.09	8.33	8.33			282	.96	41.29
Claims for compensation disallowed	1	.12	11.11				1	.09	8.33	8.33			2	.06	7.14
Claims for compensation awarded and later discontinued							3	.29	25	25	1	.62	4	.13	14.28

Disability noted on demobilization:																			
For conditions resulting from effects of gas																			
For conditions not resulting from effects of gas																			
For conditions in part resulting from effects of gas																			
For conditions, gas as a causative factor, indeterminate																			
Total																			
39	4.65	11.41	79.59	41	4.10	9.30	75.92	33	3.24	11.36	57.89	10	6.25	12.33	83.33	123	4.08	10.79	71.51
9	1.07	18.36	12	1.20		22.22	15		1.47	26.31		2	1.25		18.66	38	1.26		22.06
			1	.10		1.85	6		.59	10.52						7	.23		4.06
1	.12	2.04				3			.29	5.26						4	.13		2.32
49	5.84	11.87	54	5.40	9.53			57	5.61	13.36		12	7.50	11.61		172	5.76	11.61	
Resulting from effects of gas—																			
For pulmonary tuberculosis																			
Average period (days) from date gassed																			
24	2.86	12.50	61.53	31	3.10	9.19	75.61	24	2.36	12.29	72.72	224			10	4	.13	17.08	3.25
240			167									7	4.37	10	70	181	2.85	11.04	69.91
19	2.26	37.73	48.71	22	2.20	30.68	53.65	17	1.67	44.53	51.51	217	2.50	20	40	230	2.05	35.95	50.40
Compensations awarded and subsequently discontinued:																			
For pulmonary tuberculosis (including those by death)																			
5	.59	5.81	9	.90		8.03	20		1.96	17.09		2	1.25		8.33	36	1.19		10.61
996			905				998					1,296				985			
1	.12	1.16	5	.50		1.16	8		.78	6.83						14	.46		4.13
44	5.25	51.16	63	6.30		56.25	66		6.49	56.41		16	10		66.66	189	6.27		55.75
1,073			1,150				1,179					1,283				1,154			
37	4.41	43.02	40	4.00		35.71	31		3.05	26.49		6	3.75		25	114	3.78		33.62
86	10.26		112	11.20			117		11.51			24	15			339	11.24		
Under compensation:																			
For pulmonary tuberculosis																			
60	7.16	53.15	31.41	42	4.20	56.66	21.00	63	6.20	41.50	32.81	9	5.62	49.44	23.07	174	5.77	49.58	27.97
389			421					397				395				396			
68	8.11	20.46	35.00	9.10	26.22	45.50	79		7.77	28.34	41.14	15	9.37	20	38.46	253	8.39	25.28	40.67
358			329				391					287				325			
6	7.11	3.14	9	.90		1.50	1		.09		52	1	.62		2.56	17	.56		2.73
21	2.50	10.99	16	1.60		8.00	10		.98	3.20	3.20	8			20.51	55	1.82		8.84
7	.83	3.66	3	.30		1.50	6		.36	3.12		1	.62		2.96	17	.56		2.73
			2	.20		1.00	1												
17	2.02	8.90	20	2.00		10	15		1.47	7.81						52	1.72		.32
4	48	2.90	6	.60		3	7		.18	3.64		2	1.25		5.12	63	3.05		8.36
8	.95	4.18	11	1.10		5.50	11		1.08	3.73		3	1.87		7.69	33	1.09		3.36
191	22.79	35.03		200	20	32.55		192	18.80	49.77		39	24.37	29.20		622	20.63	38.42	
Total																			
32	3.81	16.75	33	3.30		16.50	24		2.36	12.50		3	1.97		7.60	92	3.05		14.79
67		33.07	77	7.70		38.50	67		6.59	34.80		14	8.75		38.90	225	7.46		36.17
360	42.95		446	44.60			467		45.96			60	37.50		1,333	41	4.22		
179	21.36		212	21.20			194		19.09			34	21.25			619	20.53		
3	.36		4	.40			6		.59							13	.43		
Under maximum compensation 100 per cent.																			
Under minimum compensation 10 per cent.																			
Claims for compensation not made.																			
Claims for compensation disallowed, including cases allowed vocational training only.																			
Claims for compensation pending.																			

Sources of information:

(1) A. G. O., World War Division, Personnel Records Section and Medical Section.

(2) Data furnished by the U. S. Veterans' Bureau, from January to August, 1924; no file Historical Division, S. G. O. Complete tables compiled for each gas and for the mixed gases are on file in the Historical Division, S. G. O.

deaths from disease occurring in service, none was from pulmonary tuberculosis, although the 1 in 61 days from bronchopneumonia was additionally diagnosed ulcerative laryngitis and pulmonary tuberculosis, chronic; 29 (36.70 per cent of total deaths from disease) were from pneumonia and 28 were attributable to the immediate effects of gas. Of the 35 deaths from disease after demobilization, 17 (0.56 per cent of total cases, 12.87 per cent of total deaths, and 21.51 per cent of total deaths from disease) were from pulmonary tuberculosis, 2 of which were directly attributable to gas, the primary causes of the tuberculosis in the remaining 15 being indeterminable from the records. The average period between date gassed and date of death of these 17 cases was 1,374 days, the longest individual period being 1,995 days. The report of the United States Bureau of the Census for 1920² shows that the annual death rate from pulmonary tuberculosis per 100,000 population, in the registration States of 1900, for males for the age period 20 to 24 years, is 127.6 per cent, which is equivalent to 3.84 per 3,014, the total number considered here. At this rate, the death rate would be 19.22 per cent for 5 years, which is approximately the period over which the 17 deaths from tuberculosis of this series occurred, the most recent death occurring 1,995 days after date gassed. It appears, therefore, that the number of deaths from pulmonary tuberculosis among these gassed cases is somewhat less than the rate shown by the Census report for 1920 for males 20 to 24 years of age. The office of gas as a causative factor in the deaths from disease of 21 cases is not determinable from the records, and it is possible that some of these deaths were indirectly due to gas. It should be understood that these discontinuances other than by death were due to improvement to a degree less than 10 per cent incapacity.

Of the 622 (20.63 per cent) now under compensation, at an average rate of 38.42 per cent, 174 (5.77 per cent) are being compensated for pulmonary tuberculosis, at an average rate of 49.58 per cent, and 253 (8.39 per cent) for bronchitis, at an average rate of 25.28 per cent. The smaller comparative number under compensation for pulmonary tuberculosis, appearing among those gassed by phosgene, ordinarily would indicate that phosgene was less conducive to pulmonary tuberculosis than either chlorine or mustard gas; but it is apparent that the number under compensation for bronchitis, among those gassed by phosgene, is greater than that among those gassed by either chlorine or mustard gas; then, too, the average percentage of compensation for pulmonary tuberculosis appears less among those gassed by mustard gas than among those gassed by either chlorine or phosgene gas, and it was observed in the records that among the cases gassed with mustard gas the proportion of 100 per cent compensations for bronchitis was greater than the proportion of 100 per cent compensations for bronchitis among the other two gases. It is possible, therefore, that an explanation of this difference in incidence of pulmonary tuberculosis may be reduced to a question of diagnosis, or gravity of the cases of bronchitis involved. Of the total number receiving compensation, 55 (1.82 per cent) are receiving compensation for diseases of the heart, 52 (1.72 per cent) for diseases of the nervous system, 17 (0.56 per cent) each for diseases of the eyes, and of the upper air passages. Of the total number receiving compensation, 92 (14.79 per cent) are receiving the maximum rate of 100 per cent and 225 (36.17 per cent) the minimum rate of 10 per cent. There are 1,333 (44.22 per cent) who have made no claim for compensation; 619 (20.53 per cent) were awarded compensation which was subsequently discontinued after varying periods, and 13 (0.43 per cent) claims are pending.

Among the noteworthy evidences of the effects of poison gases apparent from the results shown are: The great preponderance of effects of the respiratory organs; the comparative rarity of persistent effects on the eyes and upper respiratory passages; the greater proportion of deaths from the immediate or recent effects of mustard gas, while in its remote effects there is little or no difference from those of chlorine or phosgene; and a death rate, from pulmonary tuberculosis, over a period in excess of 5 years, less than the rate contained in the Census report for 1920 for males, from 20 to 24 years of age. The selectivity factor of those in military service is probably off-set by the proportion of colored, among whom the rate is higher, included in the Census report.

REFERENCES

- (1) Bull. No. 16, W. D., August 13, 1921.
- (2) Mortality Statistics, 1920, Department of Commerce.

SECTION III

EXPERIMENTAL RESEARCHES

CHAPTER IX

THE CHEMISTRY OF WAR GASES ^a

In ordinary life one distinguishes sharply between gases, liquids, and solids; in gas warfare this distinction does not hold, the word gas being used broadly to denote any substance, solid, liquid, or gas, which is dispersed in the air and which irritates the lungs, eyes, or skin.

From the beginning of the great war there was a steady development in gases as the means of defense against them were improved. Since chlorine (the gas used earliest in the war) attacks most substances readily, it can be stopped easily. It was soon found that a cloth steeped in sodium hyposulphite solution and mopped over the nose and mouth gave fairly satisfactory protection against the chlorine, this gas being a respiratory irritant, but it did not protect the eyes. In order to strike at this weak point, the Germans then made use of lacrymators or "tear gases," such as bromacetone and xylyl bromide, which were sent over in shell because they were not very volatile. This form of attack was met first by the use of a hood with eyepieces; later, by the introduction of regular gas masks. The hoods could be impregnated with sodium hyposulphite or other substances. The next move on the part of the Germans was to find a toxic gas which was less readily stopped than chlorine, and they made use of phosgene. This was not volatile enough to be used by itself in cylinders, and consequently it was mixed with chlorine. To stop this the British hoods and the first French masks were steeped in a solution of sodium phenolate and urotropin (hexamethylene tetramine). The British before long changed from the hood, or helmet, as it was called, to an impervious mask with a box respirator or canister attached. The air came through the canister, which contained chiefly soda-lime granules and charcoal, both of which stop gases much more effectively than the solutions in the fabric of the helmets.

There being no other gases suitable for use in cylinders, the Germans were now forced to use substances which were fired in shell and which were scattered by the explosion of the booster charge in the shell. The use of chloropierin was the next step in advance. This substance may be described as an all-round gas, having associated advantages and disadvantages from the offensive point of view. It is fairly toxic and moderately lacrymatory. It causes vomiting and therefore makes it difficult for a man to keep on his mask. It is not stopped by soda-lime, and it had the great advantage of not being stopped well by the charcoal in use in the early part of 1917. An improvement in the quality of the charcoal was necessary in order to stop chloropierin, and this was accomplished by the Allies. This improvement removed all danger from chloropierin and made the mask so good that it stopped practically all gaseous substances fairly well.

^a The data in this chapter are based, in the main, on "History of the Chemical Warfare Service in the United States," May 31, 1919, Part I, by Lient. Col. W. D. Bancroft, C. W. S., Research Division, Chemical Warfare Service, American University Experiment Station. On file, Chemical Warfare Service, Munitions Building, ⁰²¹/₂.

The introduction of the so-called mustard gas in July, 1917, changed the whole state of affairs again. This is a liquid boiling at about 217° ; it attacks the skin, causing bad burns, which may incapacitate a soldier for a number of weeks. Special ointments and special clothing were devised as a protection against mustard gas; but these were not really satisfactory at the time the armistice was signed, and the best protection had been found to be not to keep troops long in gassed areas.

That the gas-mask canister did not stop tobacco smoke was well known, and it had been found necessary to put in cotton wads in order to keep stannic chloride smokes from getting through it. The Germans took advantage of this fact and developed their so-called sneezing gas. This is a high melting solid, diphenylchlorarsine, which is dispersed, by means of high explosives, as a very fine smoke. Protection against it is provided by supplying the canister with suitable filtering pads.

A brief account will now be given of the more important gases used by the Germans and this will be followed by a discussion of some of the war gases developed by the Allies.

GASES USED BY THE GERMANS

CHLORINE

Chlorine, Cl_2 , was first used in April, 1915. It is a greenish-yellow gas with a suffocating and irritating smell. It boils at 33.6° ; the vapor pressure of liquid chlorine is 3.66 atmospheres at 0° and 11.5 at 40° . The molecular weight is 71, so that the vapor is nearly 2.5 times as dense as air (71:28.8). The density of liquid chlorine is 1.4685 at 0° and 1.4108 at 20° . It is easily prepared and easily liquefied. It is so volatile that it can be used in a cylinder or cloud attack. To prevent the cooling of the cylinders the discharge tube runs to the bottom as in a soda siphon and evaporation takes place outside the cylinder.

Chlorine is not very toxic, the lethal concentration being 2.5 mg. per liter (770 p. p. m.) for dogs on 30 minutes exposure. It is very corrosive but reacts so readily with most things that it is easily stopped. In the canister it reacts direct with soda-lime. It is also absorbed by charcoal and reacts with moisture, according to the equation $2\text{Cl}_2 + 2\text{H}_2\text{O} = 2\text{HCl} + 2\text{HClO} = 4\text{HCl} + \text{O}_2$, the hydrochloric acid being taken up by the soda-lime. Dry chlorine does not react with iron and can therefore be kept in steel cylinders. It is soluble to about 10 per cent in carbon tetrachloride. One volume of water absorbs about 2.6 volumes of chlorine at 760 mm. (reduced to 0°). In aqueous solution there is a reversible hydrolysis represented by the equation $\text{Cl}_2 + \text{H}_2\text{O} = \text{HCl} + \text{HClO}$.

Light, charcoal, and certain catalytic agents cause the decomposition of hypochlorous acid, $2\text{HClO} = 2\text{HCl} + \text{O}_2$.

Chlorine is prepared by electrolysis of an aqueous solution of sodium chloride.

PHOSGENE

Phosgene, COCl_2 , was first used in December, 1915. It is a colorless gas with a smell like musty hay. It boils at 8.2° , and the vapor pressure of liquid phosgene is 1.6 atmospheres at 20° and 3.1 at 40° . It is over three times as dense as air. The density of the liquid is 1.432 at 0° . It is not

sufficiently volatile to be used by itself in cloud attacks and is always mixed with chlorine in such cases, the mixture usually containing 20 to 25 per cent phosgene. It is about seven times as toxic as chlorine, the lethal concentration for dogs on 30-minute exposure being 0.35 mg. per liter (80 p. p. m.).

Phosgene reacts readily with water according to the equation $\text{COCl}_2 + \text{H}_2\text{O} = \text{CO}_2 + 2\text{HCl}$. Although this reaction is not reversible, phosgene is very stable when in contact with concentrated hydrochloric acid. The English physiologist, Barcroft, has found that under the conditions of his experiments, phosgene vapor is hydrolyzed only to about 10 per cent in the presence of an excess of water vapor, even though the reverse reaction does not take place to any measurable extent. It seems probable that phosgene and water react chiefly, and perhaps solely, at the surface of the containing vessel and that the reaction comes practically to a standstill when the surface becomes covered with a film of hydrochloric acid of sufficient concentration.

Phosgene reacts readily with ammonia, aniline, hexamethylene tetramine, pyridine, and many other organic compounds. When heated to 300° or so, it dissociates to some extent into carbon monoxide and chlorine. It does not react with cyanogen chloride, and the two substances can be separated by fractional distillation. The data on the corrosion of metals are contradictory, probably owing to differences in the phosgene used. Steel and Monel metal stand up well in most experiments; aluminum is resistant to phosgene containing traces of chlorine, but does not make a good showing when there is 25 per cent chlorine. Lead is usually attacked readily. On the other hand, one set of experiments showed that shell steel lost over 10 times as much as lead when submerged for 30 days at room temperature. There are apparently no data on the corrosion of metals by the mixtures used in cylinder attacks.

Phosgene can be detected by the color change in filter paper treated with dimethylaminobenzaldehyde and diphenylamine. The paper changes to yellow and then to orange with increasing concentration. When used according to directions, it will detect 1 part of phosgene per 1,000,000 of air.

In the canister, phosgene is absorbed by charcoal and reacts with the moisture in the latter to form carbon dioxide and hydrochloric acid, which are taken up by the soda-lime. Soda-lime does not absorb or decompose phosgene sufficiently rapidly to give adequate protection. The charcoal gives the activity and the soda-lime the capacity. Increased moisture in the charcoal increases its efficiency toward phosgene.

Phosgene is made by the combination of carbon monoxide and chlorine in the presence of charcoal as a catalyzer, $\text{CO} + \text{Cl}_2 = \text{COCl}_2$.

CHLOROPICRIN

Chloropicrin, CCl_3NO_2 , is a colorless liquid, boiling at 112° , and having a vapor pressure of 5.8 mm. at 0° , 14.0 mm. at 15° , and 23.8 mm. at 25° . The vapor is nearly six times as dense as air. The density of the liquid is 1.6924 at 4° and 1.6539 at 20° , the two determinations not being made by the same man. The melting point is 69.2° . Chloropicrin is not sufficiently volatile for use by itself in cloud attacks. While it has been used mixed with 75 per cent chlorine, it was usually fired in shell. It is moderately toxic, 0.8 mg. per liter (110 p. p. m.); somewhat lacrymatory, 0.016 mg. per liter, and liable to cause vomiting, thus forcing removal of the mask. It was not stopped

satisfactorily by the charcoal first used in the masks. The laboratory charcoal eventually employed was about one thousand times as effective as the earlier material.

Chloropierin is practically nonmiscible with water, and a mixture of the two boils at about 84°. It is miscible in all proportions with many organic solvents. There is a marked evolution of heat when it is mixed with methyl alcohol, ether, or acetophenone; a slight evolution of heat when mixed with isobutyl alcohol, isoamyl alcohol, or carbon bisulphide.

Chloropierin is not hydrolyzed by water, nor by cold hydrochloric, sulphuric, or nitric acid. When heated with these acids it is said to distil unchanged. Dilute aqueous sodium hydroxide does not attack it; but alcoholic sodium hydroxide decomposes it slowly, and sodium ethylate attacks it fairly readily, forming the ortho-carbonic ether, $\text{CCl}_3\text{NO}_2 + 4\text{C}_2\text{H}_5\text{ONa} = \text{C}(\text{OC}_2\text{H}_5)_4 + 3\text{NaCl} + \text{NaNO}_2$. Chloropierin can be heated for several days with aqueous ammonium hydroxide at 100° without undergoing any appreciable change. At 150°, or when heated with alcoholic ammonia, a reaction takes place in a few hours, guanidine being formed, $\text{HN}:\text{C}:(\text{NH}_2)_2$. Alcoholic potassium acetate decomposes chloropierin completely at 100° and alcoholic potassium cyanide reacts at a lower temperature, the product in this last case having the formula $(\text{CN})_2\text{C}(\text{NO}_2)_2 - \text{Cl}$. Though chloropierin is attacked very slowly by dilute aqueous sodium hydroxide, it unites readily with neutral potassium sulphite, $\text{CCl}_3\text{NO}_2 + 3\text{K}_2\text{SO}_3 + \text{H}_2\text{O} = \text{CH}(\text{NO}_2)(\text{SO}_3\text{K})_2 + 3\text{KCl} + \text{KHSO}_4$. This reaction is the basis of a quantitative method for determining the concentration of chloropierin vapor in air. A definite volume of air is passed through a neutral solution of sodium sulphite and the resulting amount of sodium chloride is determined. The data on the corrosion of metals are conflicting, but dry chloropierin apparently attacks steel but slightly and copper and lead considerably more.

Chloropierin may be detected by its giving a pink color with a suitably prepared solution of alpha-naphthol or a blue color with a different solution of beta-naphthol. A flame test with copper gauze may be used also, the appearance of a green flame showing the presence of chlorine in the flame. This is a general test and not a specific one for chloropierin. A concentration of one in a million can be detected by passing the air through a sodium ethylate solution and testing for sodium nitrate.

TRICHLORMETHYLCHLOROFORMATE

Trichlormethylchloroformate, $\text{ClCO}_2\text{CCl}_3$, is called diphosgene by the British, surpalite by the French, and superpalite by the Americans. It is a colorless, mobile liquid with a fairly pleasant sweet odor. It boils at 128° and has a vapor pressure of 2 to 4 mm. at 0° and of 10.3 mm. at 20°. The vapor is over seven times as dense as air and is twice as dense as phosgene. The density of an impure sample of the liquid is 1.687 at 0° and 1.656 at 20°. Owing to the low volatility superpalite was used only in shell and only by the Germans. The shell usually contained mixtures of superpalite and phosgene, though some duds have been found containing superpalite and chloropierin. Diphenylchlorarsine also has been found in some of the green cross shell.

The lethal concentration for dogs is 0.35 mg. per liter for exposure of 30 minutes (40 p. p. m.), but is much lower on longer exposures. Superpalite owes its importance to its high vapor density, to its persistency because of its high boiling point, and to the increased toxicity on long exposures.

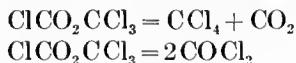
Superpalite is hydrolyzed slowly by water at room temperature and fairly rapidly at 100°, the products being HCl and CO₂, presumably according to the equation, $\text{ClCO}_2\text{CCl}_3 + 2\text{H}_2\text{O} = 4\text{HCl} + 2\text{CO}_2$.

Boiling with an aqueous solution of sodium hydroxide for half an hour decomposes it completely. Heated by itself to 300°, it is said to decompose into phosgene, but this may be the result of a catalytic action. Superpalite reacts with methyl alcohol in the cold to give trichlormethylmethoxyformate: $\text{ClCO}_2\text{CCl}_3 + \text{CH}_3\text{OH} = \text{CH}_3\text{OCO}_2\text{CCl}_3 + \text{HCl}$.

On long boiling with methyl alcohol the methoxyformate reacts according to the equation, $\text{CH}_3\text{OCO}_2\text{CCl}_3 + \text{CH}_3\text{OH} = 2\text{CH}_3\text{OCOCl} + \text{HCl}$.

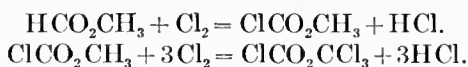
Ammonia reacts rapidly with superpalite vapor forming ammonium chloride and urea, $\text{ClCO}_2\text{CCl}_3 + 8\text{NH}_3 = 4\text{NH}_4\text{Cl} + 2\text{CO}(\text{NH}_2)_2$.

Alumina causes superpalite to decompose into carbon tetrachloride and carbon dioxide, while iron oxide and charcoal decompose it to phosgene,

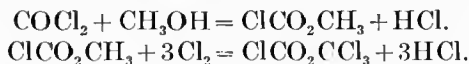


Some preliminary experiments seem to indicate that in a sealed tube at constant temperature, the decomposition of superpalite in the presence of iron oxides does not run to an end, even though the reverse reaction does not take place. This raises the question whether the Germans really put a mixture of superpalite and phosgene into their shell or whether the extremely variable concentration of phosgene may be due to the catalytic decomposition by the steel shell. There are no experiments as yet to show what effect chloropierin has on this decomposition. In the canister, superpalite is decomposed by the charcoal to phosgene, which is then decomposed by moisture. Superpalite is also decomposed readily by soda-lime.

Superpalite was probably made in Germany by chlorinating methylformate to methylchloroformate and then chlorinating this to superpalite,



While superpalite was not used by the Allies as a war gas, it has been prepared in this country for testing purposes by the action of phosgene on methyl alcohol, giving methyl chloroformate, which is then chlorinated to superpalite.



In the first stage, a possible side reaction is $\text{COCl}_2 + 2\text{CH}_3\text{OH} = (\text{CH}_3)_2\text{CO}_3 + 3\text{HCl}$, which has no toxic value and which has been thrown away in the past, although it can be decomposed by prolonged heating into superpalite and phosgene, $\text{C}(\text{Cl}_3)_2\text{CO}_3 = \text{ClCO}_2\text{CCl}_3 + \text{COCl}_2$. The chlorination of methyl chloroformate to superpalite takes place when the heated liquid is exposed to intense light while the chlorine is passed in. Nitrogen-filled lamps may be used as the source of light.

BROMACETONE

Bromacetone, $\text{CH}_2\text{BrCOCH}_3$, is a water-clear liquid which turns brown or black on standing, owing to charring. It boils with decomposition at about 126° , and the vapor pressure of the crude product is 1 mm. at 10° and 9 mm. at 20° . It is not quite five times as dense as air. The density of the liquid is given as 1.631 at 0° and 1.603 at 20° . It causes lacrymation at 0.0013 mg. per liter (0.22 p. p. m.) when pure, and at 0.0011 mg. per liter when containing 20 per cent chloracetone (Martonite), although the chloracetone is a poorer lacrymator than bromacetone. Being fairly volatile and readily decomposed, it is classed as a nonpersistent lacrymator. Troops can advance a few hours after the shelling. Bromacetone attacks steel and most other metals and must be used in shell lined with lead, glass, or enamel.

Bromacetone is only slightly soluble in water, but readily miscible with alcohol and acetone. Traces of water stabilize the product somewhat, and addition of chloracetone seems to have the same effect. There is some reason to believe that the instability is due to the presence of some impurity, but it is not known what impurity has this effect. Both the charcoal and the soda-lime in the canisters stop bromacetone.

Bromacetone can be made by passing bromine into acetone to which small pieces of marble have been added and then shaking with water and separating the bromacetone layer, which is afterwards distilled with steam. It can be made also by adding bromine dissolved in a saturated solution of potassium bromide to the acetone, or by adding bromine to a solution of acetone in 15 per cent sulphuric acid. The product usually contains some dibromacetone. These methods have not gone beyond the laboratory stage in this country. The French have manufactured a mixture of about 80 per cent bromacetone, and 20 per cent chloracetone, which they call Martonite. In order to prevent the loss of half the bromine as hydrobromic acid, they add a mixture of sodium chlorate and sulphuric acid to oxidize the hydrobromic acid. The reaction is as follows: $5\text{CH}_3\text{COCH}_3 + 4\text{Br} + \text{H}_2\text{SO}_4 + \text{NaClO}_3 = 4\text{CH}_2\text{BrCOCH}_3 + \text{CH}_2\text{ClCOCH}_3 + \text{NaHSO}_4 + 3\text{H}_2\text{O}$.

BROMMETHYLETHYLKETONE

Brommethylethylketone is a mixture of $\text{CH}_2\text{BrCOC}_2\text{H}_5$, boiling at 145° , and of $\text{CH}_3\text{COCHBrCH}_3$, boiling at 133° . It is made by brominating methylethylketone, $\text{CH}_3\text{COCH}_2\text{CH}_3$. It lacrymates at 0.009 mg. per liter (1.3 p. p. m.) and is substituted for bromacetone solely on account of shortage of acetone. Shell must be lined to prevent corrosion.

XYLYL BROMIDE

Xylyl bromide, $\text{CH}_3\text{C}_6\text{H}_4\text{CH}_2\text{Br}$, is a mixture of the ortho-, meta-, and para-compounds, and boils at about 212° . It lacrymates at 0.002 mg. per liter (0.25 p. p. m.) and is classed as a persistent lacrymator. Lined shell must be used. Both the charcoal and the soda-lime stop xylyl bromide. The mixture of the three xylenes, which is ordinarily called xylene, is heated, exposed to sunlight, and treated with bromine. Under these conditions the bromine substitutes in the methyl side chain and not in the benzene ring. Care must be taken not to carry the bromination too far, as the dibromide is of no value. Xylyl bromide is sometimes called toluyyl bromide, because the bromine substitution compound of toluene is called benzyl bromide.

DICHLORETHYLSULPHIDE (MUSTARD GAS)

Mustard gas, so-called, $(\text{CH}_2\text{ClCH}_2)_2\text{S}$, melts at 14.2° , when very pure, to a colorless, oily liquid which boils at 217° at 750 mm. The name "mustard gas" was given to it by the British soldiers, and is an unfortunate one because the compound has nothing to do with what the chemist calls mustard oil. The vapor is a little less than six times as dense as air. The vapor pressure of a sample melting at 13.8° was about 40 mm. at 140° , 30 mm. at 120° to 125° , 20 mm. at 111° , and 12 mm. at 97° . Some British data are 44 mm. at 128° to 132° and 10 mm. at 109° . The density of the liquid referred to water at 0° is 1.2790 at 15° , 1.2686 at 25° , and 1.2584 at 35° . Owing to the low vapor pressure the substance can be used only in shell and is very persistent. The Germans marked their mustard gas shell with a yellow cross.

The lethal concentration is 0.05 mg. per liter (7 p. p. m.). The liquid produces burns which appear 4 to 12 hours after exposure and heal very slowly. The vapor also causes burns, but to a much less extent. It attacks the eyes, causing conjunctivitis and temporary blindness. The percentage of deaths was rather low in mustard gas cases, only about 5 per cent; but this is not due to any low toxicity. It is because the number of casualties due to mustard gas burns was very large. A comparison, from this point of view, with phosgene, which does not burn the skin, is therefore quite improper.

Mustard gas is very slightly soluble in water, less than 0.1 per cent. It is freely soluble in alcohol, ether, chloroform, tetrachlorethane, chlorobenzene, and trioxymethylene. It is miscible in all proportions with ligroin above 19° and with kerosene above 25.6° . At a pressure of 760 mm., 100 volumes of dichlorethylsulphide dissolve 182 volumes of ethylene at 15° and 100 volumes at 95° . At 0° mustard gas dissolves about 3 per cent of dry hydrochloric acid. At room temperature it dissolves about 1 per cent of sulphur, the solubility becoming about 6 per cent at 100° . Dichlorethylsulphide is hydrolyzed very slowly by cold water and quite rapidly by hot water to thiodiglycol, which is harmless, $(\text{CH}_2\text{ClCH}_2)_2\text{S} + \text{H}_2\text{O} = (\text{CH}_2\text{OHCH}_2)_2\text{S} + 2\text{HCl}$.

Sodium perborate, hydrogen peroxide, and the dry peroxides of zinc, magnesium and sodium have only a slight effect upon dichlorethylsulphide. Sodium and ammonium sulphides react slowly in the cold, more rapidly upon warming. Calcium, sodium, and potassium hypochlorites, when present in excess, react quickly with evolution of heat. Dry bleaching powder was used by the Germans to destroy mustard gas on the ground. The sulphur is oxidized only partially to sulphate, a water-soluble sulphur compound being formed as well. Potassium permanganate reacts with mustard gas. In acid solutions about four atoms of oxygen are used up by each molecule of the sulphide. Concentrated nitric acid oxidizes the dichlorethylsulphide to the sulphoxide $(\text{CH}_2\text{ClCH}_2)_2\text{SO}$, melting at 109.50° , while fuming nitric acid carries it to the sulphone $(\text{CH}_2\text{ClCH}_2)_2\text{SO}_2$, melting at 54° .

Zinc and acetic acid or aluminum powder and sodium hydroxide destroy dichlorethylsulphide very rapidly, but sulphur dioxide, sodium thiosulphate, and sodium hydrosulphite do not react. Chlorine reacts readily, giving the symmetrical tetrachlorosulphide, which is not irritant. Sulphur dichloride reacts rapidly with mustard gas, forming the tetrachlorosulphide. It is this property which makes sulphur dichloride such a valuable reagent in the laboratory for removing mustard gas. The reaction also takes place in carbon tetra-

chloride solution and more slowly the more dilute the solution. Sodium sulphide solution reacts, forming the ring compound $S:(CH_2CH_2)_2:S$. Chloramine-T (p-toluene sodium sulphochloramine) and dichloramine-T (p-toluene sodium sulphodichloramine) react vigorously with mustard gas, forming white, crystalline compounds which are not irritating.

At ordinary temperature pure mustard gas has practically no action on aluminum, zinc, tin, lead, copper, bronze, or steel. At 100° aluminum, lead, and brass are not attacked appreciably, while copper, bronze, and steel are corroded slightly, and zinc and tin are attacked rapidly. Mustard gas can be detected by smell at about 1 part in 3,000,000; the selenious acid test is sensitive to about 1 part in 1,000,000; while a flame test has been developed which is sensitive to 1 part in 10,000,000, but is not specific, being a test for chlorine.

The Germans made mustard gas by the chlorhydrin method. Chlorine and water react to form hypochlorous acid, which combines with ethylene to give chlorhydrin, $C_2H_4 + Cl_2 + H_2O = CH_2ClCHOH + HCl$.

The chlorhydrin reacts with sodium sulphide to form dihydroxyethyl sulphide, $2CH_2ClCHOH + Na_2S = (CH_2OHCH_2)_2S + 2NaCl$. On treating with hydrochloric acid, mustard gas is formed according to the equation, $(CH_2OHCH_2)_2S + 2HCl = (CH_2ClCH_2)_2S + 2HCl$.

The Allies made mustard gas by the sulphur chloride method. Gaseous ethylene is passed into liquid sulphur monochloride contained in large iron reaction vessels, which are usually lead lined. The reaction occurs spontaneously with evolution of much heat. Sulphur is set free and the temperature must be controlled carefully in order to keep this sulphur in colloidal suspension and thus to prevent its precipitation in the solid form in the reacting vessel and the connecting pipes. The equation for the reaction may be written: $2C_2H_4 + S_2Cl_2 = (CH_2ClCH_2)_2S + S$.

It is probable, however, that sulphur monochloride dissociates to a very slight extent into sulphur and sulphur dichloride, $S_2Cl_2S + SCl_2$, and that the dichloride is the substance which reacts with the ethylene. It is certain that the reaction takes place in two stages and it is probable that the intermediate product is CH_2ClCH_2SCl . The colloidal sulphur can be precipitated with ammonia if desired.

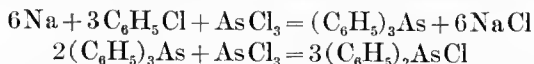
DIPHENYLCHLORARSINE

Diphenylchlorarsine, $(C_6H_5)_2AsCl$, is a solid melting at about 44° and boiling at about 330° . The vapor pressure is 25 mm. at 233° and 7 mm. at 180° . The density of the vapor is about nine times that of air. The density of the crystals is 1.4223 at 15° . It was used in shell in the presence of high explosive which scatters it as a very fine powder or smoke in the air. The Germans marked these shells with a blue cross. The lethal concentration is about 0.1 mg. per liter, but the substance is used chiefly to cause sneezing and thus to force removal of the mask, and is often called "sneeze gas." It can be detected at 1 part in 100,000,000, produces nasal irritation at 1 part in 50,000,000, and is intolerable at 1 part in 1,000,000, attacking the eyes as well as the respiratory tract. It was first used by the Germans in July, 1917. It is not soluble in water or ammonia, but is readily soluble in alcohol, ether, or benzene. It is hydrolyzed by water to $(C_6H_5)_2AsOH$ and is oxidized by concentrated nitric acid to diphenyl arsenic acid. Chlorine destroys the irritating effect of diphenylchlorarsine, probably due to formation of $(C_6H_5)_2AsCl_3$, or $(C_6H_5)_2AsOCl$.

though it is possible that the chlorine either causes the agglomeration of the smoke and causes it to be stopped by the canister. Phosgene has no such effect but phosgene containing 1 per cent of chlorine does, and it is stated that a marked increase in the capacity of the cloud is noticed.

The vapor of diphenylchlorarsine is stopped by charcoal; and the suspended substance by special filters or otherwise.

It is not known how the Germans made this compound, but it is probable that the reactions are the same as those made use of in this country and in England; the formation of triphenylarsine from sodium, chlorobenzene, and arsenic trichloride in presence of benzene, and the conversion of triphenylarsine and arsenic trichloride into diphenylchlorarsine by heating in an autoclave.



While the Germans used a large number of other gases in small amounts, the list just given includes all the really important ones, and it will now be desirable to discuss a few substances which were used or developed by the Allies.

GASES DEVELOPED BY THE ALLIES

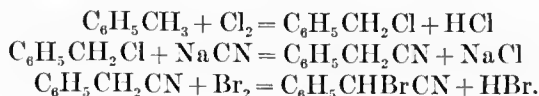
BROMBENZYL CYANIDE

Brombenzyl cyanide, $\text{C}_6\text{H}_5\text{CHBrCN}$, is a colorless solid melting at 29° . The crystals soon turn pink, owing to a slight decomposition, which does not proceed far, however. The commercial product melts at 16° to 22° , and the crystals are varying shades of dark brown, often with a marked greenish tint. The vapor pressure is given as 0.025 mm. at 0° and 0.250 mm. at 40° . The compound decomposes before the boiling point is reached, even in a high vacuum. The density of the solid is about 1.51 at 25° .

Brombenzyl cyanide is a very effective lacrymator. Most people can detect it at 0.021 parts per 1,000,000 and are lacrymated at 0.04 parts per 1,000,000 (0.00033 mg. per liter).

The compound is insoluble in water, moderately soluble in cold alcohol, freely soluble in hot alcohol, and soluble in ether, glacial acetic acid, carbon bisulphide, and benzene. It is hydrolyzed very slowly by boiling water and by cold solutions of sodium hydroxide. A cold alcohol solution of sodium hydroxide decomposes it rapidly, forming sodium bromide. It is oxidized slowly by potassium permanganate, bleaching powder, chromic acid mixture, etc. Brombenzyl cyanide attacks all metals rapidly except lead, and it corrodes lead. It would probably have to be loaded in enamel-lined or glass-lined shell. The magnesium and kaolin cements are satisfactory in presence of brombenzyl cyanide. It does not react with mustard gas. The charcoal in the American canister stops it very well; but the German charcoal appears not to be so effective.

Brombenzyl cyanide is prepared in successive steps, starting with toluene, which is converted into benzyl chloride. Benzyl cyanide is made from this by mixing with alcoholic sodium cyanide and distilling. The benzyl cyanide is brominated by treatment with bromine vapor in presence of light. All the apparatus is made of lead or is lead lined.



ETHYL IODOACETATE

Ethyl iodoacetate, $\text{CH}_3\text{ICO}_2\text{C}_2\text{H}_5$, is a colorless oil, of extremely penetrating odor, which turns brown in the air with liberation of iodine. It decomposes if boiled in the air. The vapor pressure is 250 mm. at 143° and 0.87 mm. at 30° . The density of the liquid is 1.8320 at 4° . The toxic concentration for dogs is about 1.6 mg. per liter; but the substance is primarily a lacrymator. Nine people out of ten tested were lacrymated at 0.14 parts per 1,000,000 (0.0014 mg. per liter). Owing to the scarcity of iodine, this is not a very satisfactory substance for war purposes. It was made by the English at a time when the price of bromine was very high.

PHENYLDICHLORARSINE

Phenyldichlorarsine, $\text{C}_6\text{H}_5\text{AsCl}_2$, is a highly refractive liquid boiling at 253° to 255° . The vapor pressure is 27 mm. at 142° . The substance blisters the skin much more rapidly than does mustard gas. A burn up to four days old would be judged three to four times as extensive as a mustard gas burn of the same age, and equally as severe. The burns heal more rapidly than do those from mustard gas, so that the usefulness of this liquid is not established. A 60 per cent yield can be obtained by heating triphenylarsine and arsenic chloride in suitable proportions in an autoclave at 250° for 14 hours. $(\text{C}_6\text{H}_5)_3\text{As} + 2\text{AsCl}_3 = 3(\text{C}_6\text{H}_5)\text{AsCl}_2$.

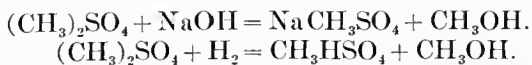
METHYLDICHLORARSINE

Methyldichlorarsine, CH_3AsCl_2 , is a colorless liquid with a powerful burning odor. It boils at 131.5° , and has a vapor pressure of about 2.2 mm. at 0° and 19.3 mm. at 35° . The vapor is between five and six times as dense as air. The density of the pure liquid is given by Richter and Byers as 1.873 at 0° and 1.81 at 35° . The toxic concentration for dogs is 0.20 mg. per liter (78 p. p. m.).

Methyldichlorarsine is miscible in all proportions with arsenic chloride, while water dissolves 29 per cent by weight and 16 per cent by volume. It is insoluble in concentrated hydrochloric acid and very sparingly soluble in the constant-boiling acid. It may be distilled without decomposition alone or with hydrochloric acid stronger than 15 per cent. Distillation with water causes a good deal of hydrolysis. Alkalies and alkali carbonates cause hydrolysis in the cold. The liquid has only a very slight action on shell steel even at 54° . The substance is stopped in the canister both by the charcoal and the soda-lime.

Methyldichlorarsine is made in three stages:

(1) Dimethyl sulphate reacts with sodium arsenite to form disodium methyl arsenite, $\text{Na}_3\text{AsO}_3 + (\text{CH}_3)_2\text{SO}_4 = \text{Na}_2\text{CH}_3\text{AsO}_3 + \text{NaCH}_3\text{SO}_4$. Possible side reactions are:



(2) Dimethyl sodium arsenite reacts with sulphur dioxide to form methyl arsine oxide, $\text{NaCH}_3\text{SO}_3 + \text{SO}_2 = \text{CH}_3\text{AsO} + \text{Na}_2\text{SO}_4$.

The bisulphite formed by the excess of sulphur dioxide must be decomposed before the third stage is carried out, as otherwise the sulphur dioxide liberated would carry off with it a large part of the methyldichlorarsine.

(3) Methyl arsine oxide reacts with hydrochloric acid to form methyldichlorarsine. $\text{CH}_3\text{AsO} + \text{HCl} = \text{CH}_3\text{AsCl}_2 + \text{H}_2\text{O}$.

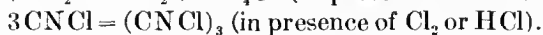
CYANOGEN CHLORIDE

Cyanogen chloride, CNCl , is a colorless liquid, boiling at 12.6° , and solidifying at about -7.3° . The vapor pressure is 444 mm. at 0° and 682 mm. at 10° . The density of the vapor is only a little more than double that of air. The density of the liquid is 1.22 at 0° . It is a good lacrymator (0.015 mg. per liter) and is highly toxic, low concentrations causing cramps in the chest and higher concentrations causing symptoms similar to those of hydrocyanic acid. Like hydrocyanic acid, there is no cumulative effect. The toxic concentration for dogs is 0.20 mg. per liter (72 p. p. m.); but dogs are the most sensitive to cyanogen chloride of any of the animals.

One volume of water dissolves 25 volumes of cyanogen chloride, 1 volume of ether dissolves 50 volumes, and 1 volume of alcohol 100 volumes. The alcohol solution decomposes, esters of carbonic and carbamic acids being formed. Sodium ethylate converts cyanogen chloride into cyanic ether, while potassium chloride solution changes it to potassium cyanide and chloride, $\text{CNCl} + 2\text{KOH} = \text{KCNO} + \text{KCl} + \text{H}_2\text{O}$.

An aqueous solution of cyanogen chloride is turned black by alkali, but is not polymerized by hydrochloric acid or chlorine. Nearly pure cyanogen chloride is polymerized to a white solid, cyanuric chloride $(\text{CNCl})_3$, by small amounts of hydrochloric acid or chlorine. When dry, cyanogen chloride does not attack iron, lead or silver, but does attack copper. If moist it attacks all these metals.

Cyanogen chloride is made by the chlorination of aqueous hydrocyanic acid $\text{HCN} + \text{Cl}_2 = \text{CNCl} + \text{HCl}$. Disturbing side reactions are:



HYDROCYANIC ACID

Hydrocyanic acid, HCN , is a colorless, mobile liquid, boiling at 26.5° . The vapor is slightly less dense than air. The toxic concentration for dogs is about 0.08 mg. per liter (90 p. p. m.), but dogs are exceptionally sensitive to this gas. The English physiologist, Barcroft, went into a gas chamber with a dog and stayed there unhurt until the dog had been killed by hydrocyanic acid. There is no cumulative effect. Neither the British nor the Germans used hydrocyanic acid. The French used a mixture called Vincennite; but there seems to be no evidence of its value.

SMOKES

In addition to the toxic gases, several substances have been used as irritant or incendiary smokes. A brief mention of the more important of these may be desirable.

PHOSPHORUS

Phosphorus is prepared by heating phosphate rock with sand and coke in an electric furnace, $\text{Ca}_3(\text{PO}_4)_2 + 3\text{SiO}_2 + 5\text{C} = 3\text{CaSiO}_3 + 5\text{CO} + 2\text{P}$.

Phosphorus comes on the market as either white (yellow) or red phosphorus. Either form burns to phosphorus pentoxide and is then converted to phosphoric acid, $4\text{P} + 5\text{O}_2 + 6\text{H}_2\text{O} = 2\text{P}_2\text{O}_5 + 6\text{H}_2\text{O} = 4\text{H}_3\text{PO}_4$.

Since one pound of phosphorus takes up 1.33 pounds of oxygen and 0.9 pounds of water, it is not surprising that phosphorus is the best smoke producer per pound of material. In addition to its use as a smoke producer, it is used in incendiary shell and for coating tracer bullets.

TIN TETRACHLORIDE

Tin tetrachloride, SnCl_4 , is a liquid made by treating tin with chlorine. It boils at 114° , and fumes in moist air because it hydrolyzes to stannic hydroxide, $\text{SnCl}_4 + 4\text{H}_2\text{O} = \text{Sn}(\text{OH})_4 + 4\text{HCl}$. It makes a better and more irritating smoke for shell and hand grenades than either silicon tetrachloride or titanium tetrachloride. It goes through the charcoal and the soda-lime; but is stopped by the layers of cotton wool in the canister. Since there is practically no tin produced in the United States, silicon tetrachloride and titanium tetrachloride have been developed as substitutes.

SILICON TETRACHLORIDE

Silicon tetrachloride, SiCl_4 , is made from silicon or from impure silicon carbide by heating with chlorine in an electric furnace, $\text{Si} + 2\text{Cl}_2 = \text{SiCl}_4$.

It is a colorless liquid, boiling about 58° and fuming in moist air owing to hydrolysis, $\text{SiCl}_4 + 4\text{H}_2\text{O} = \text{Si}(\text{OH})_4 + 4\text{HCl}$.

It is not of much value in shell, but is better on moist cool days than on warm dry ones. An ammonia cylinder and a silicon tetrachloride cylinder with liquid carbon dioxide as propellant give a first-class smoke when the jets from the two cylinders impinge. $\text{SiCl}_4 + 4\text{H}_2\text{O} + 4\text{NH}_3 = \text{Si}(\text{OH})_4 + 4\text{NHCl}$. By adding a lacrymator to silicon tetrachloride one gets a mixture which works well in hand grenades for mopping up trenches.

TITANIUM TETRACHLORIDE

Titanium tetrachloride, TiCl_4 , is made from rutile, TiO_2 , by mixing with carbon and heating in an electric furnace. A carbonitride is formed which is said to have the composition $\text{Ti}_5\text{C}_4\text{N}_4$; but the actual composition may vary from this to the carbide TiC . When these products are heated with chlorine, titanium tetrachloride is formed. This is a colorless, strongly refracting liquid which boils at about 136° , is stable in dry air, and fumes in moist air. It is said that the addition of water to form $\text{TiCl}_4 \cdot 5\text{H}_2\text{O}$ gives a good smoke and that the hydrolysis to $\text{Ti}(\text{OH})_4$ gives a poorer smoke. Titanium tetrachloride is poorer than tin tetrachloride and silicon tetrachloride in hand grenades. In the smoke funnel it is better than tin but not so good as silicon. Since it costs more than silicon tetrachloride, it would really be used only in case of shortage of the former.

CHAPTER X

PHYSIOLOGICAL ACTION OF PHOSGENE, CHLORINE, AND CHLOROPICRIN ^a

TOXICOLOGY

Among the problems submitted to the medical division of the Chemical Warfare Service was the study of the changes induced by toxic gases in the economy of animals, with a special reference to modifications in intermediary metabolism, and the determination of alleviative and curative measures.

It is obvious that in order to interpret intelligently the effects of gas poisoning upon the organism, it is essential to determine the changes, so far as possible, that the gases bring about. Inasmuch as these alterations are generally of a chemical nature, the problem must be attacked by chemical methods. The knowledge thus gained is fundamental for any measures that may be employed to prevent or alleviate the detrimental effects of poisonous gases.

In order that consistent results might be obtained, considerable attention was given to the experimental method of gassing. The technique as finally evolved was worked out in cooperation with officers of the Chemical Warfare Service. In principle it consisted of passing a mixture of gas and air through an air-tight chamber containing the "experimental animal" for a definite period at a determined rate, checking the mixture by frequent analysis of samples taken from the chamber. Unless otherwise indicated, the dog was employed as the experimental animal throughout the investigation.

The exposure of the dog to the gases elicited the following reactions, each gas differing slightly from its neighbor. The general clinical symptoms included by gassing with chlorine were, at first, general excitement, as indicated by restlessness, barking, urination, and defecation. Irritation was distinctly visible, as indicated by the blinking of the eyes, sneezing, copious salivation, retching, and vomiting. Later the animal showed labored respiration, with frothing at the mouth. Food was refused, although the animal might drink a large quantity of water. The respiratory distress increased until eventually death occurred from apparent asphyxiation. On the other hand, if the concentration of gas was not lethal the animal would present an emaciated appearance and be greatly distressed for several days, followed by ultimate recovery and return to apparently normal conditions.

Phosgene acted chiefly as a respiratory irritant, but was also a lacrymator. Very small doses, scattered in the air, caused coughing, watering of the eyes, and intense dyspnea. It differed from chlorine in that in these small concentrations its influence was limited mainly to the terminal air cells of the lungs. This effect led to edema of the lungs, accompanied by interference with the respiratory exchange and consequent cyanosis, a grave condition usually terminating in death. The first symptoms were dizziness and cyanosis on exertion. It usually required several hours for the serious symptoms to develop, and in the interval there might have been no sign of danger.

^a The data in this chapter are based, in the main, on the experimental observations made by the section on intermediary metabolism of the medical division of the Chemical Warfare Service at Yale University, account of which is found in "The Lethal War Gases," by Frank P. Underhill, New Haven, Yale University Press, 1920.

At high concentrations there was slight lacrymation and uneasiness. The pupils became clouded, but the animal showed no violent symptoms. Subsequently dogs exposed to high concentrations developed a hard cough, respiration became more and more difficult, usually there was a rattling in the throat, and death followed three to twelve hours after exposure.

Animals subjected to lower concentrations developed the same chain of symptoms which, however, were not quite so severe at first. Death occurred, as a rule, after 18 to 36 hours. After death the nostrils and trachea were filled with mucus. The lungs were collapsed and filled with mucus and blood. The slow filling of trachea and lungs accounted for the deaths which occurred 18 to 48 hours after gassing. The heart action grew weaker as death approached but persisted after all attempts at breathing had ceased.

Chloropicrin is a lacrymatory and respiratory irritant. Repeated exposure was said to cause increased susceptibility. Exposure to this gas produced coughing, nausea, and vomiting, and in large quantity could cause unconsciousness. Secondary effects were bronchitis, shortness of breath, a weak irregular heart, and gastritis. Chloropicrin could also cause acute nephritis. Liquid chloropicrin had a corrosive action on the skin, and scratches and abrasions if exposed to chloropicrin fumes invariably became septic and abscess formation sometimes resulted.

During the early part of exposure to chloropicrin the eyes were irritated, and lacrymation occurred. The mucous membrane of the nose and mouth was irritated almost instantly, the animal licking its nose and swallowing frequently. There was always increased nasal secretion and usually salivation, and in cases where salivation was not observed the animal was usually swallowing the saliva. As a rule retching and vomiting occurred 10 to 15 minutes after the beginning of the exposure with the higher concentrations. With lower concentrations the animal did not always retch. Toward the end of the exposure the animal was usually depressed, and in some cases marked paleness of the mucous membrane in the mouth was observed. The respiration was frequently affected early, being somewhat rapid in the early part of the exposure and becoming slower at the end. A tracheal rattle soon developed and respiration was labored and painful. The animal often had a bad cough, and was generally depressed. Convulsions were observed just before death. In case of survival, the dog had symptoms of bronchitis and rhinitis for a few days and then was apparently normal.

A comparison of the three gases showed quite plainly that chlorine had a very strong irritating action, the animal under observation becoming excited and in evident distress. With chloropicrin the character of the reactions produced were very similar to those of chlorine, except in being less pronounced. Phosgene, on the other hand, appeared to cause the animal no immediate distress. Instead of becoming unduly excited the dog lay quietly in the chamber and even when symptoms of poisoning appeared hyperexcitability was not present. It seemed that a certain degree of peripheral anesthesia was present, handling the animal failing to act as a stimulus to muscular activity and to cause the struggling so characteristic with chlorine and chloropicrin dogs.

TOXICITY AND LETHAL CONCENTRATIONS

The method of exposing experimental animals to definite concentrations of the gas has been indicated. The animals were always gassed singly, experience having demonstrated that when two dogs were gassed at once in the same chamber very inconstant toxicity figures were obtained. This was due to the fact that the gas mixture in the chamber showed very wide variations in composition, probably owing to the difficulty of properly controlling the flowmeter. It is possible that an extensive experience with the flowmeters might have obviated this factor. On the other hand, when the dogs were gassed singly the toxicity figures obtained were strikingly constant.

The question of the lethal concentration of the different gases for dogs was next investigated. For this purpose animals of both sexes, various breeds, ages, and states of nutrition were employed, but in every instance the dogs were considered good subjects for experimentation, none having previously undergone any experimental treatment. In all instances the animals were subjected to the action of the gas for a period of one-half hour, the rate of flow of air through the chamber being 250 liters per minute.

LETHAL CONCENTRATION OF CHLORINE

For the investigation with chlorine 112 animals were employed. The results of the study are summarized in Table 17, which shows the toxicity of chlorine gas for a one-half hour exposure at various ranges of concentrations, expressed both in milligrams of chlorine per liter of air and in parts of chlorine per million parts of air. The data from this table demonstrate that dogs gassed with high concentrations (2.53 mgm., or above, per liter) of chlorine gas usually died from the acute effects within the first 72 hours. The small percentage of animals which survived this acute stage usually recovered within a week. The dog gradually developed an appetite and appeared normal, with the exception of some emaciation and laryngitis or bronchitis, either of which could persist for some time.

TABLE 17.—*Toxicity of chlorine gas*

Concentration (mgm. Cl per liter of air)...	0. 16-0. 80	1. 27-1. 58	1. 58-1. 90	1. 90-2. 22	2. 22-2. 53	2. 53-2. 85	2. 85-6. 34
Parts Cl per million of air.....	50-250	400-500	500-600	600-700	700-800	800-900	900-2, 000
Deaths:							
First day.....per cent.....				19	17	52	71
Second day.....do.....		6	10	24	22	26	21
Third day.....do.....			10		11	9	
Total acute deaths.....do.....		6	20	43	50	87	92
Delayed deaths.....do.....	11	24	20	24	11	4	
Recoveries.....do.....	89	70	60	33	39	9	7
Survivals.....do.....	100	94	80	57	50	13	7
Number of animals exposed.....	9	17	10	21	18	23	14

At lower concentrations (1.90 to 2.53 mgm. per liter) the percentage of recoveries increased rapidly. Another condition stood out prominently at these concentrations, namely, a group of animals which survived for several days. The symptoms were loss of appetite, extreme depression, weakness, and rapidly developing emaciation. Death after this chronic condition must

be differentiated from the acute deaths, since the former were generally due to secondary factors, usually pneumonia of the purulent type. The animals in the chronic condition did not exhibit the acute symptoms, i. e., labored and distressed breathing, after one or two days. Therefore, the third day was arbitrarily chosen as the extreme limit for acute deaths.

At still lower concentrations (1.58 to 1.90 mgm. per liter) the percentage of recoveries increased markedly. The acute symptoms were much less noticeable and recovery occurred more rapidly than at higher concentrations. Concentrations above 2.53 must be regarded as lethal. Concentrations below 1.90 were rarely fatal under the conditions of these studies.

These facts led to a general classification of gassed animals into three groups: *Acute deaths*, *delayed deaths*, and *recoveries*.

Acute deaths.—Animals which succumbed to the immediate effects of the chlorine gas, namely, deaths directly induced by edema of the lungs. The majority of the deaths from this cause occurred within 24 hours after gassing, but some animals survived for 2 or 3 days. However, these animals formed a rather clearly defined clinical group, and experience has shown that all animals dying within three days could be classified together as "acute deaths."

Delayed deaths.—Animals which survived for more than three days after gassing, but which did not recover. In the majority of cases deaths classed as "delayed" resulted from secondary factors, chiefly bronchopneumonia following the subsidence of the acute pulmonary edema. This group of deaths therefore, could not be ascribed directly to the gassing, and thus fell beyond the limits of this investigation.

Recoveries.—Animals which recovered from the gassing with, in some cases, minor secondary symptoms as bronchitis, laryngitis, slight depression, or emaciation.

The delayed deaths and recoveries, therefore, together comprised animals which successfully resisted the direct effects of the gas, and could be grouped together as "survivals"; that is, having survived the acute period. With chlorine this group included a relatively large number of dogs, whereas with phosgene and chloropicrin the groups classed as "recoveries" and "survivals," were almost identical.

A study of Table 17 shows that at concentrations below 0.81 mgm. of chlorine gas per liter of air not a single acute death occurred among the dogs of the series. At concentrations between 1.27 and 1.90 mgm. from 6 to 10 per cent of the animals died acutely, but none before the second day after gassing. Concentrations between 1.90 and 2.22 and between 2.22 and 2.53 mgm. per liter gave about 50 per cent acute deaths, which were fairly equally divided between the first and second days.

Coming to concentrations above 2.53 mgm., the picture changes abruptly, about 90 per cent of the 20 animals in the series dying acutely and of these the great majority of deaths occurred on the first day. A closer analysis of the data from gassing for one-half hour at concentrations above 2.53 mgm. per liter of air shows that between 2.50 and 2.85 mgm. the proportion of acute deaths was 87 per cent, which was nearly as great as at concentrations between 2.85 and 6.34 mgm., when it reached 93 per cent. In view of this result and the fact that the proportion of acute deaths to recoveries increased rapidly and consistently as the gas concentration was increased up to 2.53 to 2.85 mgm., this

concentration must be considered as representing essentially the minimum lethal toxicity. The same conclusion was reached when the delayed deaths and recoveries were analyzed separately.

Therefore all the data from the study of over 100 dogs gassed for half an hour at various concentrations between 0.16 and 6.34 mgm. of chlorine gas per liter of air clearly indicated that the minimum lethal toxicity of chlorine gas under the conditions of the experiment was between 2.53 and 2.85 mgm. per liter.

LETHAL CONCENTRATION OF PHOSGENE

Figures relative to the toxicity of phosgene may be found in Table 18, which is a record of experiments on 327 animals. It will be noted there that the periods of death have been divided into those occurring in one day, two days, and three days, and that these deaths are called the "Total acute deaths." Beyond the period of three days death is called "Delayed death."

The concentrations employed were as follows:

- 41-50 parts of phosgene per million of air (0.17-0.21 mgm. per liter).
- 51-60 parts of phosgene per million of air (0.22-0.26 mgm. per liter).
- 61-70 parts of phosgene per million of air (0.26-0.30 mgm. per liter).
- 71-80 parts of phosgene per million of air (0.31-0.35 mgm. per liter).
- 81-90 parts of phosgene per million of air (0.35-0.39 mgm. per liter).
- 91-100 parts of phosgene per million of air (0.39-0.43 mgm. per liter).
- 101-110 parts of phosgene per million of air (0.44-0.48 mgm. per liter).
- 111-125 parts of phosgene per million of air (0.48-0.55 mgm. per liter).

From the figures given it may be seen that, as a general statement, the higher the concentration of phosgene the more acute was death, and that for the most part death occurred within the first 48 hours. If animals survived beyond the three-day period they had a very good chance of complete recovery, the delayed deaths not being especially significant.

TABLE 18.—*Toxicity of phosgene gas*

Concentration (mgm. phosgene per liter of air).....	0.17-0.21	0.22-0.26	0.26-0.30	0.31-0.35	0.35-0.39	0.39-0.43	0.44-0.48	0.48-0.55
Parts phosgene per million of air.....	41-50	51-60	61-70	71-80	81-90	91-100	101-110	111-125
Deaths:								
First day..... per cent.....	8	26	23	36	54	50	70	100
Second day..... do.....	20	13	21	19	14	11	9
Third day..... do.....	4	8	4	9	2	6
Total acute deaths..... do.....	32	47	48	64	70	61	85	100
Delayed deaths..... do.....	16	10	10	8	9	3	3
Recoveries..... do.....	52	44	42	28	21	36	12
Survivals..... do.....	68	54	52	36	30	39	15	0
Number of animals exposed.....	25	39	79	53	56	36	33	6

A point of considerable interest is the fact that the total recoveries at concentrations between 0.31 to 0.35 and 0.35 to 0.39 mgm. per liter were about the same, although very acute death, especially within a period of 24 hours, was much more marked at the higher concentration than at the lower. From these results it may be concluded that the minimum lethal concentration of phosgene is 0.31 to 0.35 mgm. per liter.^b

^b The results obtained with the higher concentration, 0.39-0.43 mgm. per liter, are difficult of explanation and apparently are anomalous.

LETHAL CONCENTRATION OF CHLOROPICRIN

The concentrations of chloropicrin employed were as follows:

- 49-69 parts of chloropicrin per million of air (0.36-0.50 mgm. per liter).
- 70-89 parts of chloropicrin per million of air (0.51-0.65 mgm. per liter).
- 91-110 parts of chloropicrin per million of air (0.66-0.80 mgm. per liter).
- 111-131 parts of chloropicrin per million of air (0.81-0.95 mgm. per liter).
- 132-151 parts of chloropicrin per million of air (0.96-1.10 mgm per liter).
- 153-172 parts of chloropicrin per million of air (1.11-1.25 mgm. per liter).

Table 19 gives results of observations on 219 dogs. From this table it may be seen that, in general, the higher the concentration of chloropicrin the more acute was death, particularly the deaths within the first 48 hours. The number of deaths occurring within 24 hours at concentrations of 0.96 to 1.10 and 1.11 to 1.25 mgm. per liter were about equal. The minimum lethal concentration of chloropicrin has been taken as 0.81 to 0.95 per liter, where 43 per cent of animals receiving this concentration ultimately recovered.

TABLE 19.—*Toxicity of chloropicrin gas*

Concentration (mgm. chloropicrin per liter of air)....	0.36-0.50	0.51-0.65	0.66-0.80	0.81-0.95	0.96-1.10	1.11-1.25
Parts chloropicrin per million of air.....	49-69	70-89	91-110	111-131	132-151	153-172
Deaths:						
First day..... per cent.....	8	9	15	30	55	52
Second day..... do.....		6	9	17	8	29
Third day..... do.....			4	6	2	3
Total acute deaths..... do.....	8	15	28	53	65	84
Delayed deaths..... do.....		3		4	2	6
Recoveries..... do.....	92	82	72	43	33	10
Survivals..... do.....	92	85	72	47	35	16
Number of animals exposed.....	12	34	46	47	49	31

A comparison of the toxicity of the three lethal gases shows that in all acute death was a prominent feature. With chloropicrin very few animals died a so-called "delayed death." With phosgene this feature of delayed death was slightly greater, but not especially prominent. It is quite evident that phosgene was by far the most toxic gas, chlorine being the least poisonous, and chloropicrin standing between. With respect to the acute effects of the lethal gases regarding the similarity of the general effects on dogs, as outlined above, and of these gases on men in the field, a striking illustration is afforded by the following paragraph from a captured German medical pamphlet:

The majority of deaths occur during the first 24 hours and in fact during the first 12 hours, with symptoms of pulmonary edema and failure of the circulation. A diminishing number of cases die on the second and third days with accentuation of the inflammatory symptoms in the lungs. The number of cases that die still later is proportionally very small. A case who has developed no severe symptoms by the third day is seldom endangered. On the other hand, the possibility of a late increase in the gravity of the case can not be excluded with certainty before the end of the first week.

**THE INFLUENCE OF THE GASES UPON RESPIRATION,
PULSE, AND TEMPERATURE****RESPIRATION**

The immediate effect of phosgene poisoning was to cause an increase in the rate of respiration and from a normal figure of approximately 20, the rate during the first few hours after gassing was found in most cases to have risen to about double the normal. In the first few hours following gassing in the animals that were not seriously affected the rate of respiration remained somewhat above normal. In the animals which were seriously affected respiration in general increased in rate but decreased in depth so that there was rapid shallow breathing. This was apparently coupled with the development of edema in the lungs of the animals. The results attained from the study of the respiration apparently did not afford a consistent index as to the condition of the animal, but a rapid shallow breathing, in many of the cases, indicated a serious condition.

The general effect of phosgene gas on the respiratory tract of the animals was not very irritating, in fact, as has been noted by other investigators, the phosgene in many cases appeared to have an anesthetic effect. The animals lay quietly unless they were in very bad condition, very little mucus was given off from the linings of the respiratory tract, and in most cases only slight salivation occurred.

The immediate effect of gassing with chloropicrin was to lower somewhat the normal rate of respiration. Within two to three hours after exposure to the gas the respiration rate regained the normal and in serious cases continued to increase so that within the first few hours a level could be reached which was considerably above the normal. The results from the study of the respiration data as far as attained did not afford a consistent index of the animal's condition.

Chloropicrin was very irritating in its effect upon the respiratory passages and as a result a large amount of mucus and saliva was given off during the first few hours subsequent to gassing. The respiratory passages became more or less clogged and the animal exhibited considerable difficulty in breathing. In many cases the nasal passages were almost completely occluded shortly after exposure to the gas, and the animal breathed through the mouth with a characteristic gasping reflex.

Immediately upon exposure to chlorine gas the respiration was markedly accelerated, reaching a high maximum within the first hour. From this time until the third hour after gassing the rate was decidedly decreased, but was still far above normal, where it remained, with some fluctuations, for the first fifteen hours. At this time most of the animals had died or were about to die. Chlorine was exceedingly irritant to the respiratory passages; almost immediately upon exposure to the gas, and for many hours thereafter, frothy or stringy saliva dropped from the mouth constantly. The quantity of fluid thus lost to the body might be quite large. Respiration was very difficult and apparently the animal had considerable discomfort but did not appear to be in actual pain.

PULSE

The immediate effect of phosgene poisoning was a decided lowering in the pulse rate. From an average normal of approximately 90 it was found that the rate would drop to about 75 beats per minute. Many cases were noted in which the rate was less than this. In general the normal rhythm was not reached until the fourth or fifth hour after gassing. However, in some cases, the pulse regained the normal rate during the first hour or so after gassing. The heart might remain at this rate or slightly higher for some hours and then there would be a gradual increase, occasionally a very rapid increase, and in the course of 10 or 12 hours in such cases the heart rate would react close to 150 beats per minute. In the animals which were less seriously affected, the rate in general remained more nearly normal than it did in those which were in a serious condition. The individual observations for the most part showed that the more seriously the animal was affected the higher would be the pulse rate. The pulse rate continued high until the animal died. There was evidence in some cases that the high rate of the heart action resulted in a circulatory failure. In such cases the pulse rate would drop very rapidly until it reached a point which might be considerably below normal and the animal died soon after.

Gassing with chloropicrin caused a sharp break in the pulse rate. It could fall to one-half, or even less, of the normal rate within the first hour. In the hours immediately following, the heart tended to regain its normal beat and in four hours or less the rate in general was normal or above.

In animals that were slightly affected by the gas the pulse rate might remain somewhat above the normal figure. In animals that were seriously affected the pulse rate returned to normal very rapidly and then in a few hours might reach a rate of 180-200 beats per minute, which might continue until death. It appeared, in some cases, that the work put on the heart at this period was too great, and suddenly the rate broke sharply and the animal died within a short time.

Immediately subsequent to exposure of an animal to chlorine gas the pulse rate fell somewhat and then steadily increased until the rate reached 150 or more between the sixth and eighth hour. Thereafter the rate decreased steadily until it usually reached a normal or subnormal value. In animals that were not fatally gassed the pulse might fall sharply within the first four hours and then rapidly rise to a very high figure, which was maintained for many hours (30 or more).

TEMPERATURE

The immediate effect of phosgene poisoning was to cause a break in the temperature. This was apparently a resultant of the lowered pulse rate and the consequent subnormal circulatory efficiency. This break in the temperature averaged about 1° C., so that the normal temperature of approximately 39° C. would fall to 38° C. within one hour after gassing. The average drop was greater in the animals which were not so seriously affected by the gassing. As the pulse rate tended to increase in the hours following gassing, so the temperature of the animal also increased, and it was found that in the great majority of dogs the temperature had reached normal between the fourth and fifth hours after gassing.

In the animals which were not seriously affected by the gas, the temperature hovered around normal, maybe slightly below or slightly above, for the next 7 or 8 hours, and then began a slow drop, so that at the end of the first 24 hours after gassing the average temperature of the dogs was about 38° C. If the animal was withstanding well the effects of the gas the temperature would slowly begin to rise and in the course of the next 21 hours or so reached the normal figure again.

In the animals which were seriously affected by the poisoning the temperature reached normal more quickly after gassing and instead of hovering around normal tended to go above, and cases have been known in which a temperature of above 40° C. was reached within the first 4 or 5 hours after gassing. The average curves showed, however, that a temperature of approximately 39.4° C. was reached in the seriously affected animals during the sixth hour after gassing. Following this the temperature began to break and the more rapidly it fell the more serious was the condition of the animal. A temperature which had fallen to 38° C. or below in from 9 to 10 hours after gassing indicated the death of the animal within less than 24 hours. The seriously affected animals which survived 24 hours after gassing showed on the average at that time a temperature about 3° C. below normal, or 36° C., and the death of the animal could be expected within less than 3 days and generally within 36 hours.

The temperature of animals after gassing with chloropicrin showed a drop which in many cases was very marked and was often as much as 2° C. The average fall was about 1° within 1 hour after gassing. In the animals that were most seriously affected the temperature continued to fall, and extreme cases were noted in which the temperature during the fourth or fifth hour after gassing was 4° C. below normal. In such cases death usually occurred within 12 hours. In the animals that were less affected the temperature after the initial drop within the first hour after gassing did not vary greatly for the next 3 or 4 hours. Beginning at about that period the temperature began to rise slowly, and in exceptional cases reached normal within 12 hours. However, in most instances the temperature after the fifth hour began to break slowly and normal temperature was not reached for one or two days. The records show that if the temperature during the first 12 hours fell much below 37° C. the animal was in a serious condition.

The temperature changes of animals after exposure to chlorine gas resembled those of the acute deaths induced by chloropicrin. With chlorine, however, the tendency was for the temperature to fall even more profoundly than was the case with chloropicrin just cited. Death usually resulted in such instances in less than 12 hours from the time of gassing.

In animals less seriously affected there was a similar initial fall in temperature which often, however, gradually returned toward the normal, the latter being attained within the first 24 hours.

EFFECTS OF REPEATED EXPOSURE

From a practical viewpoint it is important to know whether an individual becomes more or less susceptible to the gas by repeated exposure. There seems to be a rather widespread opinion that in man a single exposure to a gas greatly increases susceptibility. This view, however, is founded entirely upon general impressions, and in questions of this kind many psychological factors enter which make a clear-cut definition difficult. On the other hand, it is quite plausible to assume that a mucous membrane once extremely irritated might

be more easily thrown into an abnormal state by a weaker stimulus than would be true for a membrane which had always been normal. To test this point experiments were made with chloropicrin. The animals used had all survived an initial gassing for periods of approximately a month at least and to all appearances were normal.

If the view given above is correct this would indicate that the apparently beneficial effect of previous gassing at relatively high concentrations is due largely to the elimination of the weaker or more susceptible individuals by the first gassing. At any rate, as a result of an investigation with more than 50 animals it was indicated that so far as chlorine was concerned no evidence was obtained of any increased susceptibility. It was shown that susceptible animals were eliminated by the first gassing in proportion to the concentration at which they were gassed, and that the survivors had every chance of recovery from a second gassing at the same concentration. If, however, the second gassing was at a higher concentration, a proportionately increased percentage, could be expected to succumb.

When the problem of regassing with phosgene was investigated one was confronted with an entirely different picture, for phosgene poisoning increased the susceptibility of the animal to this gas.

CHANGES IN METABOLISM AS INDICATED BY A STUDY OF THE URINE

A problem of fundamental importance in the investigation of the physiological action of inspired gas was whether it, or its decomposition products, actually penetrated the body tissues. Were the poisonous effects of the gas due solely to its action upon the lungs or were they also due in part to absorption into the blood stream and distribution to the body as a whole? A study of the urine would perhaps give an indication in the solution of this problem. This would be true especially with chlorine inasmuch as the changes in chloride excretion might yield a decisive answer to the question.

Selected animals were observed during a six-day normal fasting period, during which time they received water but no food. At the end of each 24-hour period, except the first, the urine was collected and analyzed. The urinary picture thus obtained was taken as an index of the normal metabolism of the subject and afforded a basis for comparison with the data obtained after gassing. After this initial normal period the dogs were fed for a week and then again starved. On the second day of this fasting period they were subjected to the action of the gas, and the urine was collected at the end of each subsequent 24-hour period. This procedure was continued, as a rule, for five days, if the animal survived. The methods of urinary analysis were those commonly employed in scientific investigation.

The general effects of chlorine poisoning on the composition of the urine were as follows: The hydrogen ion concentration was increased, and there was a tendency toward augmented titratable acidity. The "organic acid" figure was markedly increased. The excretion of ammonia, total nitrogen, creatine, uric acid, phosphates, and chlorides was greater than in the normal period. On the fourth or fifth day, the output of creatine, phosphates, and chloride tended to drop below normal. Large urine volumes were frequent and protein was present in the majority of cases. The picture represented was practically the same in all experiments, though the higher concentrations of chlorine yielded more marked effects. Expressed differently, it may be stated that exposure to chlorine gas of varying concentrations caused in the dog a markedly increased protein metabolism. Typical data may be found in Table 20.

TABLE 20.—*The influence of chlorine poisoning upon the composition of the urine*

Dog No. 1

Date	Body weight	Urine											Remarks	
		Volume	Specific gravity	P _H	Titrat-able acid-ity	"Or-ganic acid"	Total nitro-gen	NH ₃ nitro-gen	Crea-tinine nitro-gen	Crea-tine nitro-gen	Uric acid nitro-gen	Phos-phates		Chlo-rides
1917	Kilos	c. c.			c. c.	c. c.	gm.	mgm.	mgm.	mgm.	mgm.	mgm.	mgm.	
NORMAL (BEFORE GASSING)														
July 23	-----	96	1.064	6.9	57	-----	3.25	136	181	0	13	528	900	
24	-----	76	1.029	6.0	31	-----	2.55	131	186	0	12	58	81	
25	16.0	55	1.049	6.0	44	-----	2.84	176	166	0	17	127	53	
26	-----	67	1.043	5.9	65	-----	3.28	202	156	0	15	187	31	
27	-----	66	1.044	6.0	49	-----	3.17	176	152	0	14	142	33	
AFTER FIRST GASSING														
[1.47 mgm. per liter for one-half hour Aug. 6]														
Aug. 6	15.6	82	1.072	6.5	84	-----	4.31	163	147	0	22	391	120	
7	-----	93	1.046	6.1	62	-----	4.67	307	152	96	20	214	640	
8	-----	61	1.047	5.9	51	-----	2.28	149	130	39	17	146	635	
9	-----	39	1.063	5.9	61	-----	1.54	75	131	3	14	192	125	
10	16.2	45	1.042	5.9	37	-----	2.10	146	120	4	13	113	58	
11	15.6	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	
AFTER SECOND GASSING														
[2.08 mgm. per liter for one-half hour Aug. 27]														
Aug. 27	16.7	304	1.023	6.3	127	-----	6.00	272	172	141	50	589	165	Protein.
28	-----	406	1.016	5.7	74	-----	4.13	298	156	175	58	271	2,016	
29	-----	108	1.032	5.6	89	-----	2.93	230	157	48	35	274	150	
30	-----	73	1.043	5.8	80	-----	2.86	196	148	14	31	257	144	
31	-----	58	1.053	5.8	77	-----	2.23	131	139	3	22	247	150	
NORMAL (BEFORE THIRD GASSING)														
Oct. 9	17.0	94	1.044	6.0	94	-----	3.87	188	159	62	25	346	68	
10	-----	101	1.047	6.3	89	-----	3.74	123	159	43	23	372	163	
11	-----	95	1.047	6.1	97	-----	3.47	135	159	68	20	379	343	
12	-----	99	1.042	6.4	86	-----	3.11	116	155	59	18	355	386	
13	-----	82	1.044	6.6	70	-----	2.57	121	154	53	17	387	286	
AFTER THIRD GASSING														
[2.05 mgm. per liter for one-half hour Oct. 22]														
Oct. 22	16.0	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	
23	-----	166	1.034	6.6	49	-----	4.40	105	131	90	25	398	160	
24	-----	150	1.038	6.2	81	-----	4.71	298	149	202	27	368	858	
25	-----	114	1.040	6.1	67	-----	3.47	200	130	102	21	266	1,253	
26	-----	74	1.050	6.1	67	-----	3.03	84	128	10	22	307	90	
27	-----	77	1.041	6.1	64	-----	2.96	153	115	0	17	272	19	
NORMAL (BEFORE FOURTH GASSING)														
Nov. 27	-----	76	1.054	5.6	81	17	2.94	162	143	25	18	319	73	Protein.
28	-----	91	1.040	5.5	76	3	2.98	163	143	45	17	322	63	Do.
29	-----	71	1.042	5.4	76	12	2.72	136	144	50	14	288	48	Do.
30	-----	65	1.048	5.8	74	18	2.55	62	145	17	14	298	92	Do.
Dec. 1	-----	79	1.040	5.7	58	10	2.57	102	148	11	16	247	59	
AFTER FOURTH GASSING														
[2.60 mgm. per liter for one-half hour Dec. 10]														
Dec. 10	16.8	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	
11	-----	154	1.060	6.4	103	32	7.53	232	181	129	29	723	159	Protein.
12	-----	418	1.022	5.9	122	39	6.23	503	177	288	29	411	2,000	Do.
13	-----	122	1.050	5.7	127	58	5.42	395	148	162	29	344	1,200	
14	-----	105	1.039	5.5	77	24	3.86	236	139	63	24	228	155	
15	15.0	84	1.039	5.4	59	19	3.20	197	139	6	23	199	11	

In order to determine whether the increased protein metabolism was a secondary manifestation of a profound disturbance in the carbohydrate metabolism, the glycogen content of the liver was estimated by Pfluger's method. Determinations were made eight hours after gassing. The results were compared with control determinations, made on normal dogs that had fasted for corresponding periods of time. The data, as given in Table 21 show that the amount of glycogen in the liver was not materially affected by gassing at high concentrations (2.53 to 2.85 mgm. for half an hour).

TABLE 21.—*Chlorine experiments*

	Percentage of glycogen in the liver	
	Normal dogs	Dogs gassed early on second day of fasting period
Killed second day of fasting period.....	0.24 .63	0.24 (dog No. 402). .42 (dog No. 401).
Killed third day of fasting period.....	.13 .26 .62	.12 (dog No. 400). .36 (dog No. 399).

Since the increased elimination of nitrogenous substances was not accompanied by a complete removal of the glycogen in the liver and therefore could not be attributed to utilization of protein in place of carbohydrates, it was indicative of destructive processes within the tissues. Possibly it was to be associated with autolytic decomposition in the lungs. In harmony with this idea was the fact that the maximum output of nitrogen fell on the second day after gassing, which was synchronous with a crisis in the lung condition.

The increased acidity of the urine and the augmented excretion of ammonia, acid phosphates, and "organic acid" all indicated acidosis, a condition which was intensified by the disturbance in protein metabolism. That the acidosis was not primarily dependent upon the augmented protein metabolism was indicated by the conditions that obtained in dogs gassed at low concentrations.

The chloride picture characteristic of severe gassing showed chloride retention during the first 24 hours, followed by increased elimination, the maximum output usually falling on the second day. This condition was intimately associated with the concentration of the blood, the period of retention being synchronous with the period of blood concentration and the subsequent increased excretion occurring when the blood returned to a more dilute condition. The increased chloride output in the urine probably can not be accepted as evidence of chlorine absorption during gassing.^c This was corroborated by the data from the chloride content of the blood and tissues. Moreover, the urine analyses failed to show any proportionality between the concentration of the gas administered and the chloride increment eliminated in the tissues.

^c In this connection search was made for free chlorine in the blood and plasma of dogs before and after gassing. The inorganic chlorides were first determined by the method of McLean and Van Slyke. Samples of blood were also ashed with CaO and Na₂CO₃ and the chlorides determined in the fusion mixture. This procedure obviously would convert any free or organically combined chlorine to chloride and permit its determination as such. No significant difference was found between the two sets of analytical results. Also quantitative examinations of the protein-free filtrate from the plasma or blood for free chlorine, by means of the reaction with KI and starch paste, were equally negative. If free chlorine occurs in the blood of gassed animals it is in traces too small to admit of detection by the methods employed. It is obvious, therefore, that chlorine in appreciable amounts does not exist in the blood other than as ionized chloride, and accordingly that direct chlorine absorption by the blood is not a significant factor in gas poisoning.

Dogs gassed at a moderate concentration of phosgene, 60 to 70 parts per million of air (0.26 to 0.31 mgm. per liter), showed the following metabolic changes: The nitrogen metabolism was increased during the second 24 hours after gassing, paralleled by a very high excretion of creatine during that period. The chloride output was very high in the first 24 hours, low in the second, and high in the third, gradually returning to normal on the fifth day. The phosphate output was very high during the first 24 hours, then gradually decreased until it reached the normal value during the latter part of the experimental period. The sum of the daily phosphate excretion during the period was about the same as that of the normal period. Throughout the interval there was no evidence of diuresis, and the hydrogen-ion concentration was not affected. The "organic acids" were unchanged and remained practically constant for both the normal and the experimental periods.

Dogs gassed at a higher concentration of phosgene, 90 to 100 parts per million of air (0.40 to 0.45 mgm. per liter), presented a picture similar to those gassed at a moderate concentration, except that the chloride elimination was not as high during the first day. With lower concentrations of phosgene, 40 to 50 parts per million of air (0.17 to 0.21 mgm. per liter), the typical changes observed at moderate concentrations were present, although the extent of alterations was less marked. Tests for various abnormal constituents of the urine gave no evidence of a pathological condition.

With chloropicrin the nitrogen metabolism was increased on the second day, although in some cases it began to increase on the first day, resulting in an augmented output of total nitrogen, ammonia nitrogen, uric acid nitrogen, and creatine nitrogen. Chloride output was seldom above the normal figure. This was especially true in dogs moderately gassed. (Table 22.)

TABLE 22.—*The influence of chloropicrin poisoning upon the composition of the urine*

Dog No. 94													
NORMAL													
Date	Volume	Specific gravity	P _H	Titrat-able acidity	"Organic acid"	NH ₃ nitrogen	Total nitrogen	Creati-nine nitrogen	Creat-ine nitrogen	Uric acid nitrogen	Phos-phates	Chlo-rides	Protein
1918	c. c.			c. c.	c. c.	mgm.	gm.	mgm.	mgm.	mgm.	mgm.	mgm.	
July 23	145	27	6.1	79	17	69	4.12	179	0	10	382	120	
24	360	18	5.9	89	32	101	4.28	152	0	12	335	104	
25	255	15	5.8	92	23	92	4.37	154	0	14	364	60	
26	275	19	5.8	101	50	111	4.23	150	2	15	347	270	+
27	260	12	5.8	76	17	104	(?)	146	3	13	324	70	Trace.
Sept. 10	230	30	5.5	175	60	347	5.49	116	114	40	488	¹ 640	

GASSED SEPTEMBER 10, 9 TO 9.30 A. M.

[Concentration, 97 (0.70 mgm. per liter). Weight, 13.2 kilograms]

Sept. 11	105	60	5.9	155	16	282	4.22	114	148	71	795	664	
12	110	42	5.9	82	53	244	4.33	106	160	52	342	480	
13 ²													
14			5.8	71	24	202	2.98	112	44	37	342	390	

Dog No. 95

NORMAL

July 23	90	41	6.0	60	13	57	3.64	133	8	10	320	150	
24	90	49	5.9	104	27	61	3.89	127	0	12	378	162	
25	(50?)	24	5.7	90	20	106	4.25	113	0	15	343	172	
26	100	50	5.6	120	23	102	4.06	105	0	14	425	830	
27	80	46	5.7	90	17	102	3.49	105	3	14	326	200	
Sept. 10	240	28	5.7	174	34	372	5.06	102	51	33	668	¹ 660	

¹ Diet.² Sample lost.

TABLE 22.—*The influence of chloropicrin poisoning upon the composition of the urine—Con.*

GASSED SEPTEMBER 10, 9.30 TO 10 A. M.

[Concentration, 103 (0.75 mgm. per liter.) Weight, 9.6 kilograms]

Date	Volume	Specific gravity	pH	Titrat-able acidity	"Or-ganic acid"	NH ₃ nitrogen	Total nitrogen	Creati-nine nitrogen	Crea-tine nitro-gen	Uric acid nitrogen	Phos-phates	Chlo-rides	Pro-tein	Blood
1918	c. c.			c. c.	c. c.	mgm.	gm.	mgm.	mgm.	mgm.	mgm.	mgm.		
Sept. 11	135	60	6.0	172	32	290	5.55	92	153	71	864	550	+	
12	135	48	6.2	88	32	176	5.63	85	181	45	460	296	-----	
13	175	35	5.9	82	30	314	5.65	81	152	31	365	180	-----	
14	145	48	6.0	107	44	204	5.55	78	136	30	484	236	-----	

Dog No. 133

NORMAL

Oct. 4	50	44	5.8	35	13	118	2.05	67	4	11	159	Trace.	-----	
5	45	38	5.8	45	15	136	1.92	67	4	10	178	Trace.	-----	
10	45	32	6.0	30	11	90	1.51	66	1	12	142	190	-----	
12	50	38	5.9	45	10	104	1.60	65	4	7	202	190	-----	
17	45	40	5.8	35	11	106	1.40	67	3	12	147	150	-----	

GASSED OCTOBER 21, 9.40 TO 10 A. M.

[Concentration, 123 (0.89 mgm. per liter.) Weight, 6.8 kilograms]

Oct. 22	95	44	6.9	37	26	168	3.88	67	88	30	396	100	+	
23	180	-----	5.4?	138	29	279	4.78	65	138	30	413	560	-----	
24	115	38	6.1	80	19	334	4.95	56	110	25	323	40	-----	
25	100	-----	6.0	51	7	228	3.92	58	52	31	240	20	-----	
26	70	37	5.9	51	4	132	2.51	50	7	12	223	Trace.	-----	

Dog No. 165

NORMAL

Sept. 24	315	25	5.7	96	88	213	5.88	111	108	17	588	400	-----	
25	125	35	6.1	74	29	216	3.67	100	64	19	365	80	-----	
26	140	40	5.8	119	63	347	5.07	92	77	21	417	200	-----	
27	220	27	6.0	133	40	416	6.55	96	96	24	548	280	-----	
28	300	32	5.9	172	39	456	7.65	95	107	29	735	280	-----	

GASSED OCTOBER 7, 9 TO 9.30 A. M.

[Concentration, 116 (0.84 mgm. per liter.) Weight, 9.7 kilograms]

Oct. 8	190	50	6.1	165	7	392	8.50	83	171	34	953	280	-----	
9	325	42	6.1	239	37	615	12.50	70	223	40	1,062	440	-----	
10	385	42	6.0	293	46	575	15.30	55	240	52	1,250	560	-----	
11	375	46	6.2	260	46	538	16.25	53	334	48	1,140	620	-----	
12	-----	-----	6.0	212	59	451	13.95	45	373	26	882	450	-----	

Dog No. 135

NORMAL

Sept. 17	40	55	5.3	46	17	80	1.78	60	15	22	166	60	-----	
18	50	50	5.4	47	21	98	1.73	54	11	19	149	Trace.	-----	
19	40	42	5.5	36	8	32	1.50	53	19	17	140	Trace.	-----	
20	35	52	5.5	51	19	88	1.59	51	13	18	176	Trace.	-----	
21	40	52	5.5	-----	-----	84	-----	52	28	26	176	75	-----	

GASSED SEPTEMBER 30, 8.40 TO 10 A. M.

[Concentration, 111 (0.81 mgm. per liter.) Weight, 5.5 kilograms]

Oct. 1	45	54	5.8	60	14	118	1.76	-----	-----	-----	280	50	-----	
2	45	40	7.4+	-----	Cystitis.	-----	-----	-----	-----	-----	109	300	-----	
3	50	32	7.4+	-----		-----	-----	-----	-----	-----	116	75	-----	
4	85	21	7.4+	-----		-----	-----	-----	-----	-----	147	40	-----	

The phosphate elimination was increased greatly during the first 24 hours, often being double the normal figure. In most dogs that died within a day or two after gassing the phosphate output during the first 24 hours was only slightly above normal, and when this was found to be the case it was quite certain the animal would not survive. The titratable acidity between P_H 4.9 and P_H 7.4 ran parallel with the phosphate output, showing that this was a simple titration of the "buffer" reaction of the phosphates. The volume of the urine, hydrogen ion concentration, and "organic acids" showed little or no change as a result of gassing.

Gassings at a low concentration showed in general, the same picture as those of a moderate concentration, except that the changes were less marked. Generally the chloride output was a little higher. Gassings at a high concentration showed a picture similar to that at a moderate concentration, but the effects were somewhat prolonged.

Kidney efficiency tests were run on some dogs inasmuch as it had been asserted that chloropicrin might injure the kidneys. In the cases tested no decreased renal function could be detected.

A comparison of the excretion under the influence of the three gases showed that in all three instances nitrogenous metabolism was definitely increased, the various partitions of nitrogen running more or less parallel curves. In certain instances the increased output was most evident on the first day subsequent to gassing, in other cases the second day showed the greatest excretion. Chloride elimination was very markedly increased in some instances, as in the case of chlorine gassing, or only of slight significance as with chloropicrin, or again it might assume a widely divergent curve as with phosgene. Chloride excretion was undoubtedly linked with the changes in the development of edema; the chloride output, therefore, will be discussed more fully in connection with the development of pulmonary edema (pp. 333-342).

Acidosis might or might not have been present as indicated by changes in the hydrogen ion concentration, titratable acidity, and "organic acid" figures. These results make it evident that there was, therefore, no essential relationship between the increased nitrogen output and acidosis.

• Creatine excretion was quite prominent but seemed to follow no definite course. Apparently it was not associated with lack of carbohydrates,¹ as for example with chlorine poisoning, nor could its appearance in the urine be ascribed to a condition of acidosis² since in neither phosgene nor chloropicrin poisoning was there any indication of such a state. It was possible, however, that it might have been due to tissue changes induced in the lungs whereby disintegration occurred with the formation and subsequent elimination of creatine. By such a process both creatine excretion and increased nitrogenous metabolism would be explained, although it must be admitted that the reactions involved are by no means clear. It is quite significant that a second exposure to a gas rendered an animal neither more nor less susceptible as judged by the influence upon nitrogenous metabolism. So far as investigated there was little evidence that the lethal gases, employing chlorine as an example, were absorbed by the blood stream. At most only the merest traces were absorbed. The damage to the organism was therefore localized upon the respiratory tract.

ALTERATIONS IN BLOOD CONCENTRATION

Even a slight experience with gas poisoning led to the recognition that changes in blood concentration must occur. The evidences for such an impression were not prominent in the early stages, but as time passed it became quite apparent that the blood assumed a sticky, concentrated consistency, attempts to draw blood from a vein, for example, being attended with great difficulty. The character of the blood at this period exerted a definite detrimental influence upon the rate of circulation, reacting in time to impede the heart action, and later on even to interfere with the proper blood supply to the tissues. Under these conditions the tissues consequently suffered, and normal metabolism, therefore, was undoubtedly distinctly altered.

The changes in blood concentration have been studied extensively in this investigation, since it has been assumed that such alterations were quite suffi-

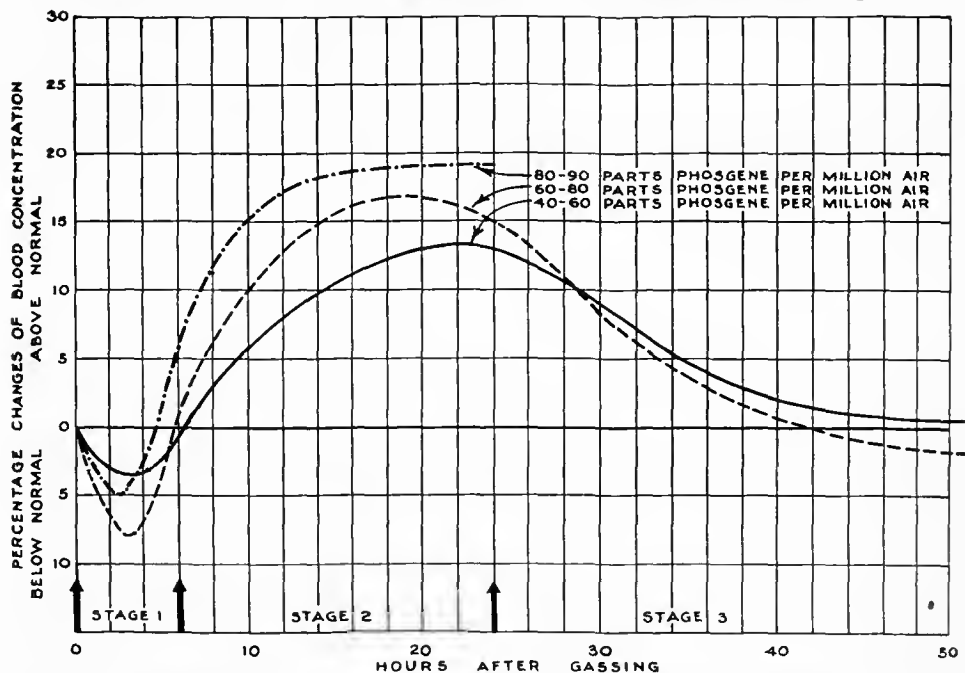


CHART VI.—Changes in total solids of blood after phosgene gassing, showing characteristic differences in the three gas concentrations selected

cient to explain many of the phenomena associated with gas poisoning. From the fact that observations have been made most intensively with phosgene, the results obtained with this gas will be presented first.

An inspection of Chart VI shows that at first the blood usually contained less solid matter than normally. This condition was maintained for several hours (stage 1). Later concentration began and rapidly assumed a maximum (stage 2), after which there was a gradual return (stage 3) to the normal level. The results showed very characteristic differences between the three gas concentrations selected. At 80 parts per million and above there was a very rapid recovery from the preliminary dilution, the normal being regained within 4 to 5 hours. The succeeding concentration was correspondingly rapid, reaching a maximum at 12 to 14 hours and was at a level 18 to 20 per cent

above the normal. Practically all of these dogs died during the second stage so that the third stage was not represented at this concentration.

With 60 to 80 parts of phosgene per million of air, stage 1 was prolonged beyond that at the higher concentration and the dilution persisted for 4 to 6 hours. The succeeding increase in the total solids also developed more slowly and was not so great, being only 16 to 18 per cent at 18 hours. More of these dogs survived the acute period and stage 3 appeared in the curve. The return to normal was practically complete by the forty-fifth hour. At the lowest concentration studies, 40 to 60 parts per million, the changes were still less in degree. The dilution period extended over 6 to 8 hours and the maximum concentration of 12 to 14 per cent was not gained until 21 to 22

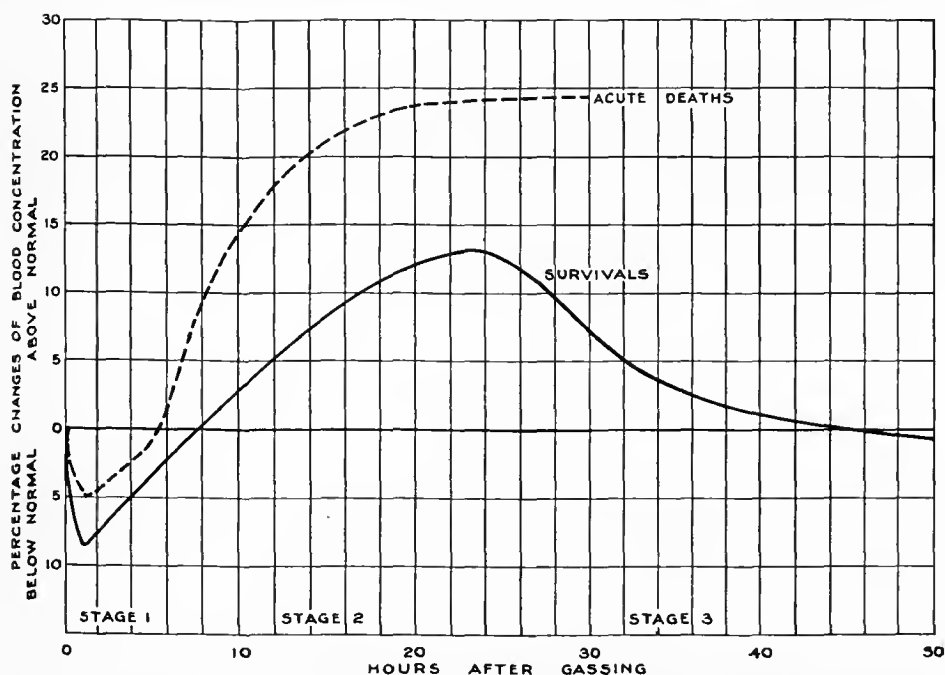


CHART VII.—Changes in total solids of blood after phosgene gassing, showing characteristic differences in the dogs that died acutely and those that survived the acute period

hours after exposure. Stage 3 was very similar to that with the intermediate concentration. Compared to the other two series, but a very few dogs in this group died.

A study of the average results outlined above would indicate a very distinct relationship between the phosgene concentration and both the rate and degree of change in the blood. As has been mentioned before, practically all the dogs in the first group died acutely, while but very few died in the last group. The dogs in the second series were about equally divided between those that died acutely and those that survived the acute period.

Careful analysis of these results indicates (Chart VII) that within each group the changes in the blood concentration showed characteristic differences, depending upon the ultimate fate of the animal. In dogs that died acutely the period of dilution was short and the normal was regained within

three to five hours. This was followed by an extremely rapid concentration that reached a maximum of 22 to 23 per cent over the normal 15 to 16 hours after gassing. All these dogs died during this period of greatest blood concentration.

The survivals show a different picture (Chart VII). The initial period of the reaction was slower, up to the sixth to tenth hour. Owing to the marked variation among individuals no distinction could surely be made between the acute deaths and survivals on the basis of the degree of dilution during this primary stage. The difference in time was marked. The great difference, however, came in the second stage, for the dog that ultimately recovered showed a very much slower development of the blood change and, in addition, the concentration was not nearly so marked, 12 to 15 per cent 22 to 24 hours after gassing. Following this came the stage of recovery, which has already been discussed.

These two types of classification with the reaction characteristic of each hold throughout the range of gas concentration studied. On the basis of this generalization it may be pointed out that the apparent correlation between response and phosgene concentration in the previous experimental series was due to the relative predominance of two separate types of reaction and not to the gradual change in the type of reaction by individual animals.

From these graphs it is quite apparent that three distinct stages may be recognized as occurring in the blood solids subsequent to phosgene poisoning.

The first stage is apparently one of dilution of the blood as evidenced by a decrease in the blood solids. This dilution is greatest one to three hours after gassing and the total solids have returned to normal by the fifth to eighth hour. The cause of this sudden decrease in blood solids is not entirely clear.

The second stage is one of blood concentration. The total solids of the blood increase rapidly to a value far above the normal and remain stationary at this level for several hours. In the dogs gassed at 90 parts per million the average value for the total solids increased up to a maximum of 25 per cent 10 hours after gassing and remained at approximately that level until the death of the dog. In those animals gassed around 70 parts per million the average value does not reach a maximum until some $17\frac{1}{2}$ hours after gassing, and even at this time the value is lower (23 per cent) than in the case of the higher gas concentration. The speed of blood concentration and the degree are both greater with the higher gas concentration.

The third stage marks the gradual return of the blood solids to the normal level.

Owing to the greater density of the red corpuscles of the blood as compared with the plasma any change in the relative amounts of corpuscles and plasma will cause a corresponding change in the total solids. The observed changes in the blood solids, therefore, might have been due either to an increase in the plasma volume during the first stage, followed in the second stage by a decrease and with no change in the erythrocytes; or else to the withdrawal of erythrocytes from the circulation in the first stage, and a later reintroduction. According to Lamson³ such changes are possible through the mediation of the blood sinuses of the liver. If the first of these possibilities is correct then the blood volume should be increased during the first phase and decreased later when concentration occurs. The reverse would be true in the second case.

Eyster⁴ reports that radiographs taken during the early stages of phosgene poisoning show a dilated heart, but without an increased plasma volume. On the other hand, in the second stage the heart is markedly decreased in size.

From the foregoing it is evident that the changes in the concentration of the blood as determined by total solids gives one a method of following the condition of the animal in this respect.

The changes in concentration might equally well be followed by the determination of the hemoglobin. Hemoglobin determination is much more rapid, less blood is necessary, and the method is even more accurate than the more cumbersome total solid determination. Accordingly, a comparison has been made between the hemoglobin content and the total solids of the blood. From this it may be concluded that the two curves are similar but not parallel, and that the degree of change in the hemoglobin at all periods after phosgene poisoning is much greater than is true for the total solids. The hemoglobin, therefore, is a much more delicate indicator of the animal's condition than is the total solids. It has been employed to estimate the changes in blood concentration.

A series of hemoglobin determinations was made upon a comparatively large number of dogs gassed with phosgene at concentrations varying from 41 to 80 parts per million of air (0.17 to 0.35 mgm. per liter). On the basis of these studies the following different types of individual reactions, together with the probable fate of the animal, may be outlined:

Type I.—The reaction of the animal was slight, there being a variable degree of dilution followed by a return to the normal hemoglobin value. Stage 1 alone was apparent in this case, the concentration being absent. The recovery of the animal was uninterrupted after the passage of the dilution.

Type II.—This type followed the usual stages of blood change, all three stages being present. The concentration in the second stage was relatively moderate, varying up to 140 per cent of the normal. Under these conditions the animals recovered.

Type III.—This type was differentiated from the second type by the degree of concentration of the blood. Concentration of over 140 per cent was usually fatal. Death usually occurred in the second stage.

The fate of the animal was dependent on two factors: (1) The degree of the concentration of the blood, and accordingly the extent of the edema, and (2) the individual resistance. In general, however, it was found that a concentration of 140 per cent marked the mean between the two conditions. Hemoglobin readings above this indicated the probable death of the animal; below this, the recovery.

Type IV.—This type was characterized by the absence of any dilution following gassing. The concentration appeared immediately, or within the first two or three hours. The blood changes in this case were rapid and extreme, and were usually followed by early death.

Earlier in this chapter it was stated that on the basis of the changes in the total solids the animals could be separated into two groups, one of acute deaths, and a second of survivals. These two classes are practically synonymous with the reaction Types II and III, as outlined above. On the basis of the greater number of animals studied it has been possible, in addition, to characterize Types I and IV.

These are the changes in the blood as indicated by the hemoglobin readings. The individual type of reaction seems to be characteristic of no particular gas concentration, as examples of each type were found at all concentrations studied. With the increasing toxicity of the higher gas concentration, greater proportions of the animals showed reaction in order of Types III and IV, while at the lower concentration Types I and II predominated. The number of animals studied at each gas concentration was not great enough to permit of a percentage analysis. In the discussion of the result at each gas concentration, however, this factor of the different types of reaction must be kept in mind. In Table 23 are given data showing the average figures obtained when the results are divided into (1) recoveries, (2) acute deaths, and (3) delayed deaths.

TABLE 23.—*Hemoglobin changes in the blood in phosgene poisoning*

Number of dogs	Average recoveries				Average acute deaths				Average delayed deaths			
	21	26	10	7	4	9	10	7	3	3	2	5
Concentration	41-50	51-60	61-70	71-80	41-50	51-60	61-70	71-80	41-50	51-60	61-70	71-80
Hours												
0-1	96	94	88	94	89		93	99		91	93	94
1-2	90	91	90	81	89	91	88		92	97		88
2-3	92	92			90	96	97	104	91		97	
3-4	92	94	87	86	90	98		105	93	103		93
4-5	93	94	89	91	102	108	98			99	104	
5-6	98	96	90	92	113	111		109		101		93
6-7	99	98	96	89	116	124	98		91	109		
7-8			98					117			109	93
8-9	105	107				131	112		106	114		
9-10				94	139			136				95
10-12	110	112	114	115		135	133		118	118		
12-14	110	115	117		144	147	135	138	121		115	112
14-16	116	117		117		152	132	137	119	139		
16-18	114	119	119		166	153			119		153	123
18-20	120	124	115	113		150	135	138	108	154	140	
20-22	119	120	108						105			122
22-24	109	113		112					104	130	155	
24-26	112	116		113								
26-28									90	140	115	
28-30				106								
30-32											129	

Dogs gassed at 41 to 50 and 51 to 60 parts phosgene per million of air were affected about equally, i. e., 72 per cent survivals and 28 per cent deaths, and 69 per cent survivals and 31 per cent deaths, respectively. The average hemoglobin picture shown by these two concentrations was almost identical. The first stage showed a dilution of 90 per cent of the normal hemoglobin in the second hour, this being followed by a gradual increase until the normal concentration was reached between the seventh and eighth hours. There was then a gradual concentration of the blood until the maximum of 125 per cent hemoglobin was reached in the nineteenth hour. The blood began then to dilute and reached its normal concentration about the thirty-sixth hour.

As the concentration was increased (61 to 70) the toxicity was markedly changed: Recoveries 45 per cent, deaths 55 per cent. The time factor in the average hemoglobin curve was slightly changed, but the curve as a whole was not altered. The blood diluted to 87 per cent of the normal concentration one hour after gassing and remained constant until the fifth hour. The blood reached its normal concentration in the ninth hour and continued to concentrate until a maximum hemoglobin concentration of 120 per cent was reached in the seventeenth hour. The return to normal then followed.

At the concentration of 71 to 80 parts per million phosgene the recoveries totaled 37 per cent and deaths 63 per cent. Following gassing there was a minimum dilution of 81 per cent after two hours, this being followed by a gradual increase until the tenth hour. Between the ninth and eleventh hours there was a marked increase of 20 per cent—a jump in two hours from below normal to its maximum concentration (116 per cent). The hemoglobin curve remained constant until about the twenty-fifth hour and then began its return to normal.

From the above discussion, the following facts are evident:

1. The blood was most dilute between the first and third hours after gassing.
2. The return to normal after the dilution took place sooner at low than at high concentrations.
3. The time of maximum concentration of the blood during stage 2 depended on the phosgene concentration; the higher the gassing, the sooner is this point reached.
4. The average maximum concentration for recovered animals was about 120 per cent of normal hemoglobin.

ACUTE DEATHS

The acute deaths have been classified as those dogs dying within 72 hours after gassing. The number of dogs dying within a few hours was relatively small, so that an average curve was not indicative of great accuracy. The individual type of hemoglobin curve may be discussed to better advantage.

The most common type of curve was one in which there was a significant dilution followed by a very marked rise in hemoglobin. The time when the concentration began varied from 3 to 10 hours after gassing and was not dependent on the concentration of the gas or the dilution of the blood during stage 1. Another type which invariably proved fatal in phosgene poisoning was an immediate concentration of the blood. The faster the blood concentrated, so much the sooner did the animal die. In certain instances, a dilated heart caused an acute or delayed death without any sign of significant blood concentration. This, however, was seldom seen.

With chlorine too few experiments were made to warrant more than the most general statements relative to blood concentration changes. The data, however, allow one to be certain that the course of blood concentration alterations, as determined by estimation of the total solids, paralleled the curve obtained by determination of the hemoglobin values. These data also indicate quite clearly that the period of blood dilution, that is,—stage 1 in phosgene poisoning—was either very slight and short lived or lacking altogether, and that the significant feature relative to the blood changes under discussion in chlorine gassing was the almost immediate tendency for concentration and the rapid development of this to a high maximum. (Chart VIII.)

The striking feature in blood changes as indicated by total solid determination after chloropicrin gassing was the usual absence of the first or dilution stage which characterized phosgene. In surviving dogs the blood steadily concentrated and attained its maximum about 10 hours after gassing. Very gradually the blood then became less concentrated until about the fortieth hour it had usually reached its normal value, and became then, for a time, less concentrated than normal.

On the other hand, 20 of the 58 chloropierin dogs studied showed a dilution period corresponding to the first stage in phosgene. This lasted for a variable interval, but was usually less than two hours, often less than one-half hour in length. In all but three cases the maximum dilution value was found in blood collected within the first hour after gassing. No animal showing this dilution died. The only two animals able to survive gassing above 1.09 mgm. per liter exhibited this dilution stage.

The maximum concentration was about the same as in phosgene, averaging 113 per cent of normal. The extent of concentration was to a certain degree dependent on the gassing strength, as it will be seen that the blood of animals gassed below 0.80 mgm. per liter failed to become as concentrated as in animals gassed above this value.

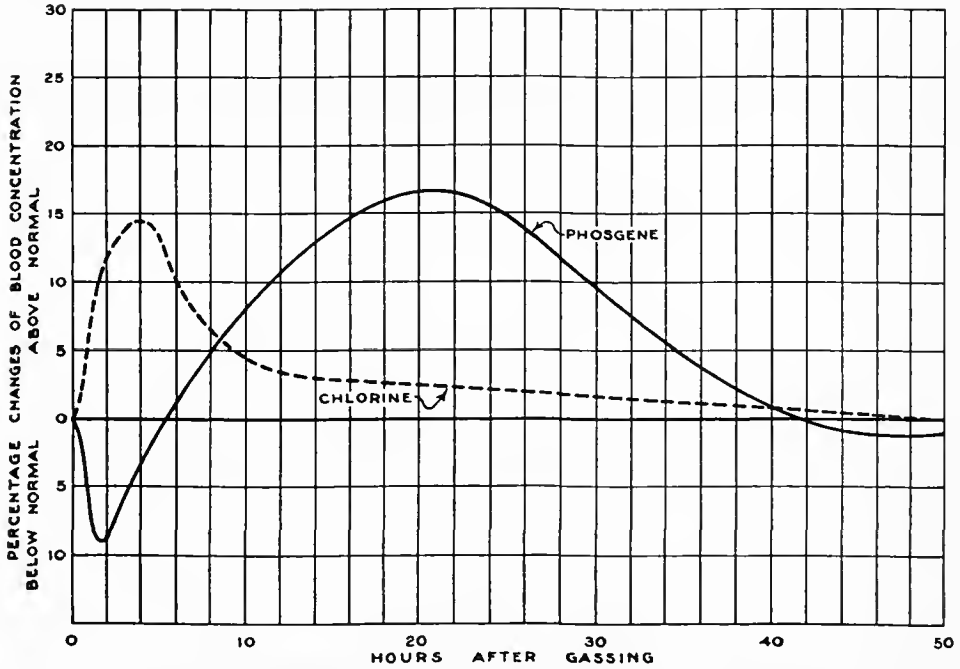


CHART VIII.—Comparison of the changes in total blood solids of dogs gassed with phosgene and those gassed with chlorine

Since, from the standpoint of treatment, the time relations of blood concentration are important, a comparison is made in the table between the effects of phosgene and chloropierin:

Average time at which maximum concentration is attained (hours)

	Recoveries	Early deaths
Phosgene.....	19 (average of 27 dogs).....	13 (average of 17 dogs).
Chloropierin.....	10 (average of 38 dogs).....	7 (average of 7 dogs).

Extreme limits of time at which maximum concentration is attained (hours)

	Recoveries	Early deaths
Phosgene.....	4-30.....	5.5-28.
Chloropierin.....	4-18.....	3-18.

The concentration was attained earlier in chloropicrin, but the variation in time was wide. In dogs which suffered early death from chloropicrin gassing, the rise to a maximum concentration value was swift. In several cases a concentration above 130 per cent normal was attained within five hours. After reaching the maximum concentration the animal usually, though not always, died within a short time, (five hours). A comparison of the relationship between the total solid curve and that of the hemoglobin may be seen by inspection of Chart IX.

If one draws characteristic curves of blood changes induced by the three gases, the diagram in Chart X would be the result. The most striking feature of the blood in relation to exposure to the lethal war gases is the marked change



CHART IX.—Comparison of total solids and hemoglobin after chloropicrin gassing

of concentration, which varies characteristically both in degree and time with the different gases. The significance which it is believed attaches to this phenomenon will be discussed in succeeding pages.

THE RED AND WHITE CELLS OF THE BLOOD

A brief study was carried through of the influence of the lethal gases upon the red and white cells of the blood and in certain instances comparison was made of the changes in the red cells and the hemoglobin.

At first observations were made with chlorine, relative to the influence of gassing upon the red cells, over an extended period; that is, cells were counted on successive days. In later work the red cell estimations were made more frequently, at intervals of hours instead of days (Chart XI). From the

data at hand it is indicated that almost immediately after chlorine gassing there occurred a characteristic rise to a high maximum of both red cells and hemoglobin. The graphs, which may be plotted from the data, more or less parallel each other. The increase in the red cell count, however, was usually somewhat greater than that of the hemoglobin value. The approximate parallelism for these two elements of the blood leads to the conclusion that the increase was apparent rather than actual. Stated differently, the apparent changes in the red cell count and the hemoglobin figures are to be referred to changes in the concentration of the blood and can not be accepted as evidence for the intrusion of new cells into the blood stream.

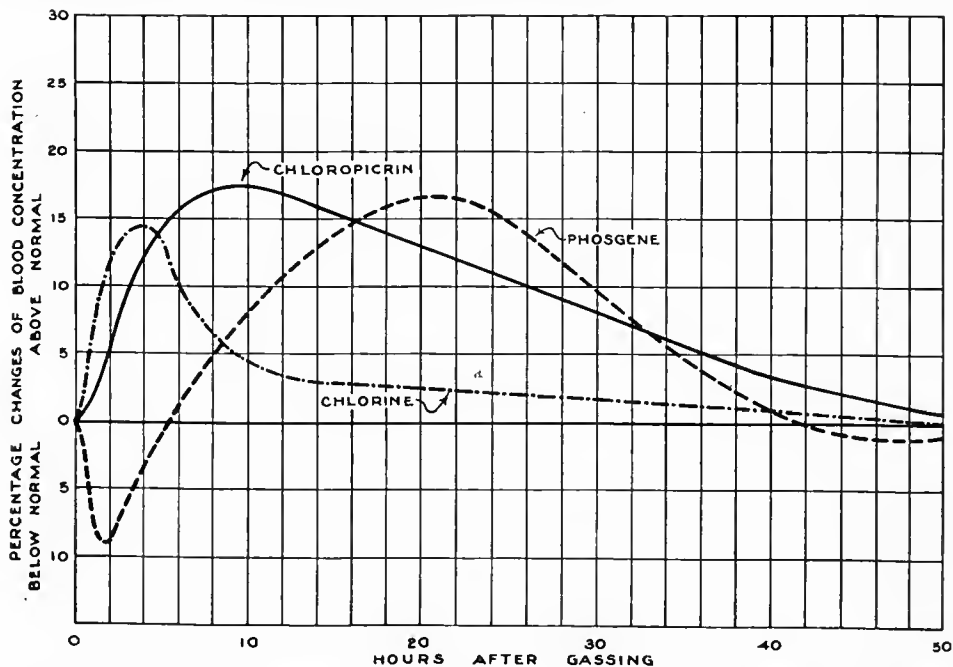


CHART X.—Comparison of the characteristic changes of blood solids induced by chlorine, phosgene and chloropicrin gases

With phosgene a similar conclusion must be drawn with respect to alterations in the number of red cells. Shortly after gassing the cells diminished in number and later rose far above the normal value, in harmony with the observed changes in blood concentration, namely, a period of dilution shortly subsequent to exposure to the gas followed by an interval when the blood becomes highly concentrated.

Chloropicrin gassing produced changes in the red cell content and hemoglobin values of the blood somewhat analogous with those induced by chlorine and in entire accord with what might be anticipated by one with a knowledge of the alterations in blood concentration induced by chloropicrin. (Chart XII.)

The data for white cell counts of the blood are incomplete in that no determinations were made with either phosgene or chloropicrin. However, a fairly extensive study was made with chlorine, the results of which follow.

Leucocyte counts were made on animals gassed with chlorine in concentrations from 0.33 mgm. to 6.32 mgm. per liter, with variable intermediate concentrations.

LOW CONCENTRATIONS

Animals gassed at extremely low concentrations (i. e., 0.18 mgm. per liter) exhibited a slight leucocytosis within three to five hours after gassing, which was followed by a return to normal almost immediately, except in cases where the animal developed a slight bronchitis. The counts were not followed beyond the third day subsequent to exposure to the gas. (Table 24.)

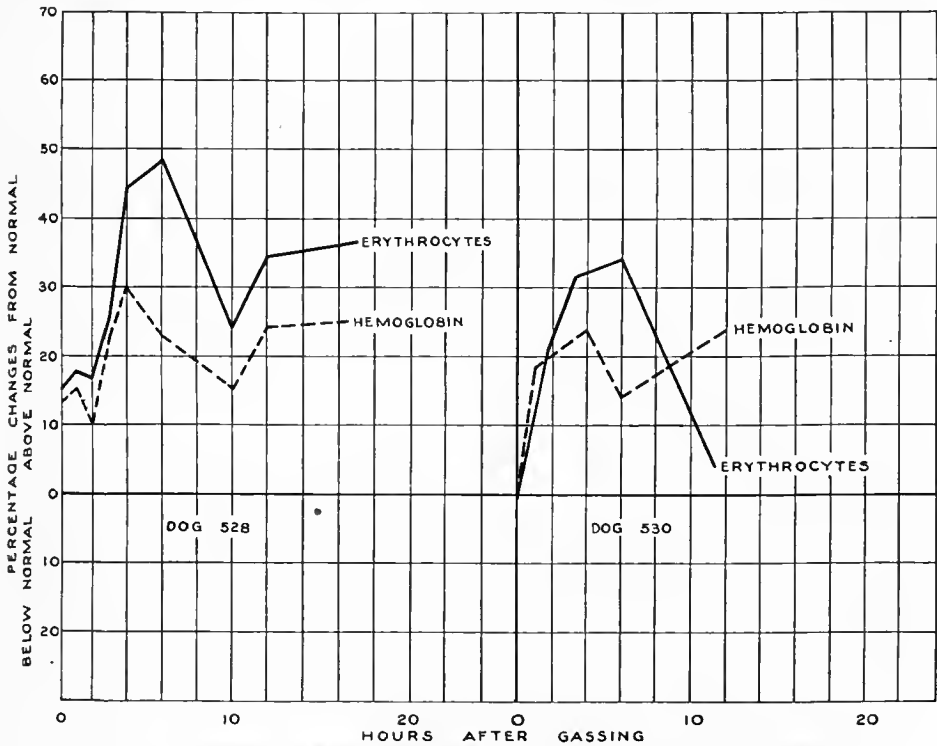


CHART XI.—Comparison of erythrocytes and hemoglobin content of blood after chlorine gassing

TABLE 24.—*The influence of chlorine gassing upon the leucocyte count*

Dog No. 525

[Gas concentration, 0.17 mgm. per liter]

Hours	Leuco- cytes	Percent- age normal	Hours	Leuco- cytes	Percent- age normal
Normal.....	16,000	100	7.....	23,600	147
1.....	10,500	66	23.....	24,000	150
2.....	9,700	61	24.....	23,000	144
3.....	14,000	87	25.....	22,500	140
4.....	18,800	117	25.....	25,000	156
5.....	25,300	158	27.....	14,800	93
6.....	22,200	139	28.....	14,800	93
7.....	22,200	139	28.....	17,600	110
8.....	23,000	144	29.....	17,600	110

Animal developed a slight bronchitis.

TABLE 24.—*The influence of chlorine gassing upon the leucocyte count—Continued*

Dog No. 526

[Gas concentration, 0.18 mgm. per liter]

Hours	Leuco- cytes	Percent- age normal	Hours	Leuco- cytes	Percent- age normal
Normal.....	6,000	100	6.....	10,880	182
2.....	6,400	106	7.....	12,000	200
3.....	4,800	80	9½.....	8,600	143
1½.....	4,800	80	12½.....	7,000	117
2½.....	8,200	136	24.....	6,000	100
4.....	8,600	143	25.....	7,700	128
4½.....	9,000	150	26½.....	5,000	84
5½.....	9,800	163			

Recovered immediately.

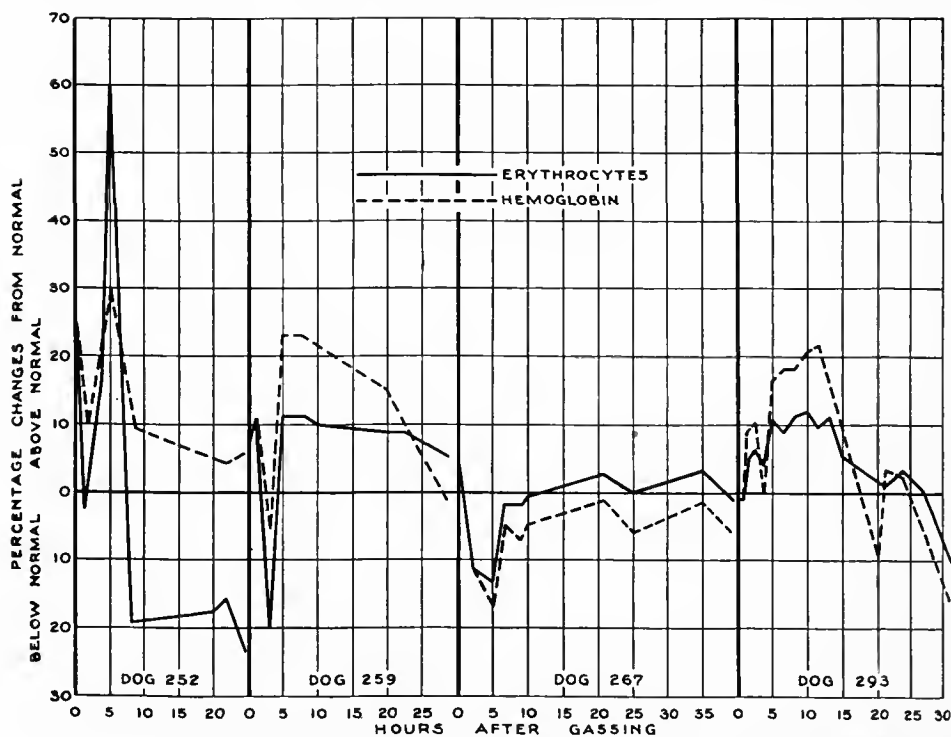


CHART XII.—Comparison of erythrocytes and hemoglobin content of blood after chloropicrin gassing

MODERATE CONCENTRATIONS

A detailed study of the changes in leucocytes was made in a series of six dogs gassed at concentrations varying from 1.23 to 2.21 mgm. per liter. Three of the dogs died, showing upon autopsy different stages of pneumonia, while two survived, passing through a stage indicating bronchopneumonia, considerable time elapsing before their full recovery.

The extent of the leucocytosis varied greatly, but showed a typical picture in any case. One dog showed very few symptoms and gave the same picture as a dog gassed at very low concentration, i. e., a slight leucocytosis and a return to normal the next day. The remaining dogs that recovered with pulmonary complications developed a moderate leucocytosis, which continued for several weeks, followed by a return to normal on complete recovery.

The fatal cases in this series showed typical curves which corresponded to the condition of animals gassed at very high concentrations. There was one type which developed an extreme leucocytosis, followed by a fall in count before death, and another in which not even a moderate leucocytosis appeared. In the latter, autopsies revealed severe cases of purulent bronchopneumonia. It may be assumed, therefore, that the development of continued moderate leucocytosis (about 200 per cent) was essential for the protection of the organism in cases where animals had been gassed at a moderately high concentration.

HIGH CONCENTRATIONS

Animals of the last series were gassed at very high concentrations, far above the lethal dose. This procedure was followed in order to see if it were possible to diagnose a fatal case of chlorine poisoning from the leucocyte count. Four distinct types of curves were observed: (a) In one case an extremely high leucocytosis was followed by death a few hours after gassing, and in another a gradual fall in count for several days, after which death resulted. (b) A moderate leucocytosis followed by a sudden drop in count on the day after gassing. (c) A failure of the organism to develop leucocytosis, in which case death resulted in about three hours after gassing. (d) A slow development of a leucocytosis followed by marked fluctuations in count, death occurring within 10 hours.

DIFFERENTIAL COUNT

A partial study of the differential picture showed that leucocytosis was caused solely by an increase in polymorphonuclear cells, the lymphocytes and mononuclear cells playing no part. The eosinophiles disappeared from the circulation for a short time several hours after gassing.

The data presented above may be restated from the standpoint of whether or not the dog recovered from the chlorine poisoning. Dogs that recovered showed two types of curves: (a) After mild gassing a slight leucocytosis (100 per cent) followed by quick return to normal; (b) after lethal concentrations of chlorine, a moderate leucocytosis (300 per cent) persisting for several weeks.

Dogs which exhibited the following leucocytotic condition invariably died: (a) A leucocytosis; (b) an unstable fluctuation in the leucocyte count during the first few hours after gassing; (c) a moderate leucocytosis followed by a marked drop (acute and chronic cases); (d) an extreme leucocytosis during the first few hours after gassing.

DEVELOPMENT OF PULMONARY EDEMA

Pulmonary edema is a very prominent feature of the effects of the lethal war gases on the animal organism. To its development attaches great significance in any explanation of the detrimental influence of a gas. Equally important is a consideration of the subject when attempts are made to define the cause of death in the circumstances under discussion.

The lethal war gases are all substances eminently irritant to living tissues, and it must be accepted that the irritation produced by a gas is the initial step in the development of edema. In response to the first irritative stimulus, tissue fluid finds its way to the injured area in an apparent attempt toward

repair or alleviation of the injury. It is conceivable that if damage to the tissue is only slight such a procedure would result in the passage to the damaged area of only a small quantity of tissue fluid. According to this view the degree of response with respect to the local deposition of tissue fluid would be in direct ratio to the extent of injury. On the other hand, it is equally plausible to assume that this reaction may reach a breaking point at a certain degree of stimulation whereby the whole mechanism governing the exudation of tissue fluid is thrown out of control so that the response to the stimulation becomes overwhelming. Under these conditions a reaction which in its initial function may be regarded as beneficent eventually becomes a direct menace to continued existence on the part of the mechanism as a whole merely by interposing mechanical difficulties in the way of respiration and circulation.

It is not proposed in this place to discuss in detail the underlying principles of edema production. Rather an endeavor will be made to correlate so far as possible various observations that have been carried through in this investigation with the development of pulmonary edema. At this time, therefore, attention is called to the development of edema of the lungs in its time relations; the correlation of pulmonary edema with changes in blood concentration; the association of edema with chloride and fluid exchange in tissues and the blood, and the relation of edema to vascular permeability.

EDEMA AND ITS TIME RELATIONS

In connection with the determination of the toxicity of phosgene for dogs a relationship was observed between the time of death and the concentration of the gas to which the animal had been exposed. In general the greater the concentration the sooner the occurrence of death. Accordingly, in this series, attention was confined to a concentration somewhat below the lethal (70 parts per million; 0.31 mgm. per liter), and to one somewhat above lethal concentration (90 parts per million; 0.40 mgm. per liter). In all cases a standard time of exposure for 30 minutes was used.

The dogs were killed by strychnine injection at intervals after exposure and samples of tissue were taken from different parts of the lung. An effort was made to secure as composite a sample as possible and to reduce to a minimum the loss of exuding edema fluid during sampling. There was always slight loss, particularly with very wet lungs, so that the results may not have been quite as accurate as when the entire lung was dried. The error, however, was negative rather than positive and the degree not sufficient to compensate for the difficulties of analysis by the latter method. The samples for the determination of the total solids in the blood were drawn at regular intervals by needle from the jugular vein. All samples were carefully dried to constant weight at 105°.

The total solids of the lung (Charts XIII and XIV) showed a rapid and extreme decrease indicating the production of an intense edema of the most marked type. This was most noticeable in dogs Nos. 481 and 479, killed at eight and nine hours after gassing. In these two animals the total solids of the lung fell to 8.6 and 7.1 per cent from a normal value of about 21.4 per cent. Assuming that the decrease in total solids was due to the influx of water alone into the lung these values would represent the influx of 150 and 200 cubic centimeters, respectively, of water per 100 grams of original tissue, a truly

enormous increase. In view of the fact that the edema fluid contained most of the constituents of plasma and that no allowance was made for these, the actual inflow would have been, therefore, greater than that here calculated.

The experimental series was small in view of the variation among individual animals, but, a careful examination of the curves (for example, Chart XIV) shows that in general the animals gassed at a concentration of 90 parts per million (0.40 mgm. per liter) showed a given total solid content 4 to 6 hours before those gassed at a concentration of 70 parts per million (0.31 mgm. per liter). At a given time the total solid content was $1\frac{1}{2}$ to $2\frac{1}{2}$ per cent lower in the dog gassed at the higher concentration.

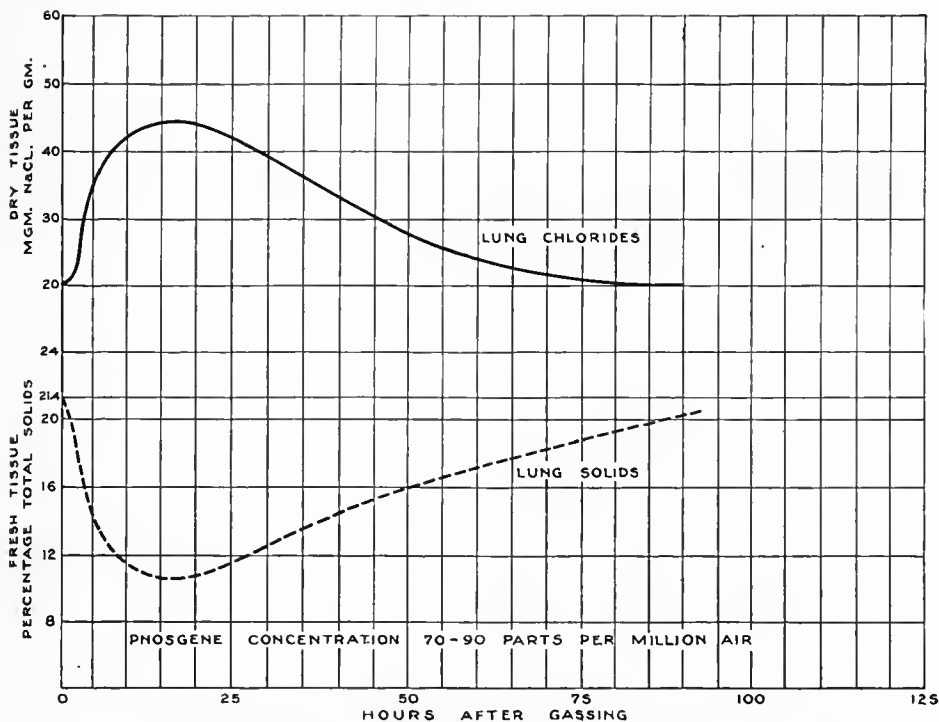


CHART XIII.—Changes in the chlorides and total solids of the lungs after phosgene gassing

A maximum degree of change was present in both sets of analytical results from 10 to 25 hours after gassing. After this time there was a more gradual return to the normal lung condition.

Analysis of lungs of dogs subjected to chlorine gas showed an immediate influx of water to a marked degree. The water of the lungs gradually subsided if the animal survived a sufficiently long period.

With chloropicrin (Chart XV) the water content changes of the lungs were very significant.

The changes in the lung indicated the rapid production of a marked pulmonary edema and its gradual subsidence with all three gases. The rapidity of the production of this edema depended in part, at least, upon the concentration of the gas employed and there were indications that there was a direct relationship between gas concentration and the degree of edema.

EDEMA AND BLOOD CONCENTRATION

In Chart XIV a comparison is made between the rate and extent of edema production and the changes in the blood solids in phosgene poisoning. The courses of the two processes are fairly synchronous, the development of edema corresponding with a fair degree of accuracy to the concentration of the blood. The only explanation for the initial dilution of the blood is that at first fluid passed more rapidly into the blood than it could pass from the blood into the lungs. In general the blood returned more rapidly to the normal level than was true for the lungs. In the latter instance, however, there was a possibility of interfering secondary factors, such as pneumonia, which might complicate the matter.

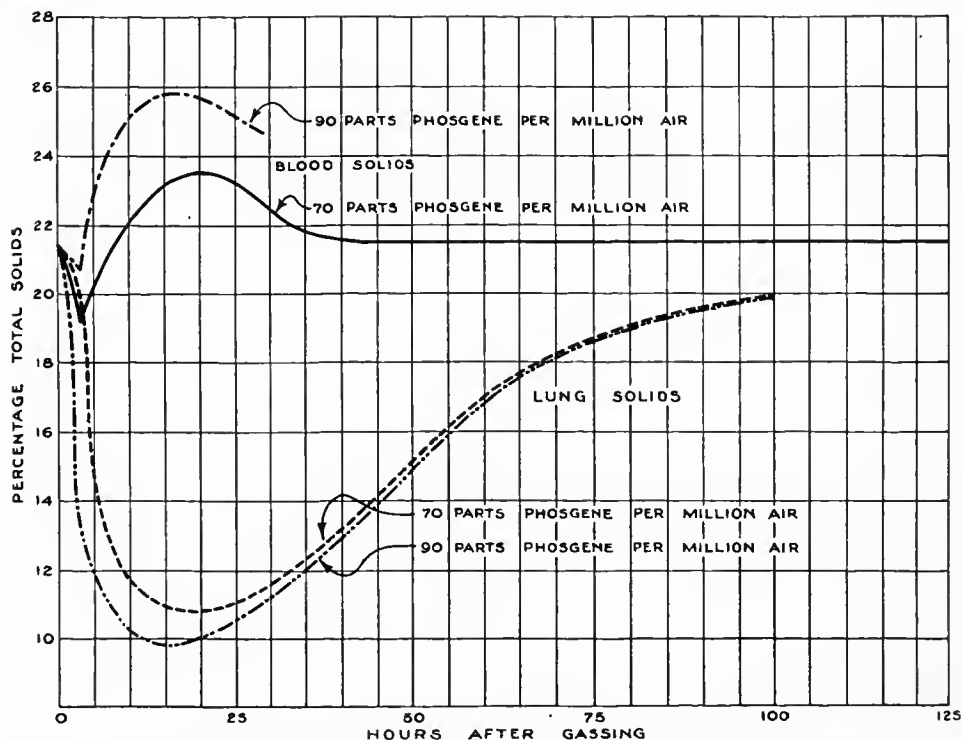


CHART XIV.—Changes in the total solids of the blood and lungs after phosgene gassing

From the data of fluid changes in the lungs, and blood concentration alterations respectively, what has been concluded relative to phosgene applies equally well to chlorine. To even a greater extent is this true for chloropierin (Chart XV.)

From the data represented it may be concluded that for the production of edema of the lungs induced by all three gases, fluid is drawn from the blood. Moreover, since it has been shown that the hemoglobin and total solids have similar types of curves *the estimation of hemoglobin may be employed to follow the course of blood concentration and hence in general to act as a criterion of the development, or stage, of pulmonary edema.*

EDEMA AND CHANGES IN SALT CONTENT OF BLOOD AND LUNGS

In any study of the production of edema the question of possible disturbances in the salt relationship is at once raised. In an effort to secure a partial elucidation of this problem a study was made of the chloride content of the blood and lungs of dogs gassed with phosgene. No study was made in this connection with chloropicrin.

In this investigation attention was confined at first to concentrations of 90 and 70 parts of phosgene per million of air, i. e., slightly above and slightly below the lethal concentration. Blood chlorides were estimated by the method of McLean and Van Slyke. The chloride content of the lungs was determined in the dried tissue used for the study of the total solids. The method of analysis was a modification of the McLean and Van Slyke procedure.

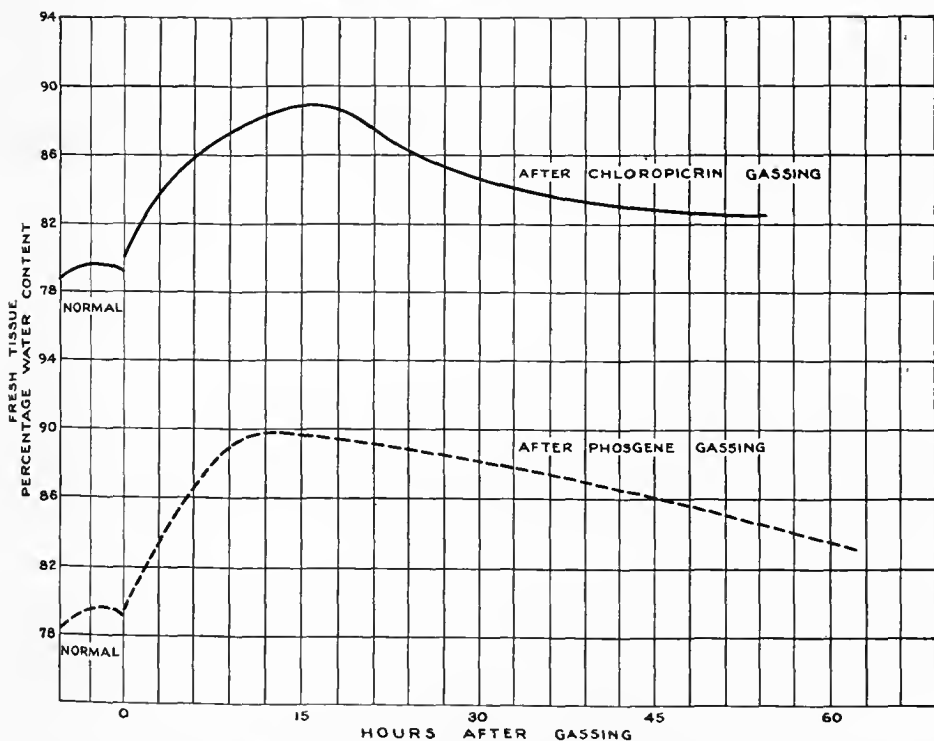


CHART XV.—Water content of lung tissue after chloropicrin and phosgene gassing

In normal starving dogs the chloride content of the blood plasma was approximately constant from day to day, but there was a wide variation among individuals. The results have been expressed in terms of the percentage of the normal value. Since it was found that the plasma and whole blood chlorides underwent parallel changes, only the plasma chlorides were determined. More uniform alterations were obtained when the animals were starved for 48 hours before gassing than when inanition was for a period of 24 hours only. Owing to the small experimental series no distinction was made between animals starved for different periods or gassed at the different concentrations, the discussion being confined to the average of the entire experimental series. The results of these observations are expressed graphically in Chart XVI.

There was practically no change in the plasma chlorides during the first four hours after gassing. Between the fifth and sixth hours, however, there was a marked and rapid drop in the blood chlorides. This drop reached a minimum at about the twentieth hour, and from then on the blood chlorides showed a gradual increase during the first two days after gassing until about the fiftieth hour when they gradually returned to normal. During the period of blood dilution there was practically no change in the blood chlorides, indicating that the diluting fluid must have been isotonic with blood plasma. The blood chlorides, however, dropped sharply at about the time the concentration of the blood first became marked.

It has already been shown that blood concentration was due to the passage of fluid from the blood into the lungs. Examination of the lungs, furthermore,

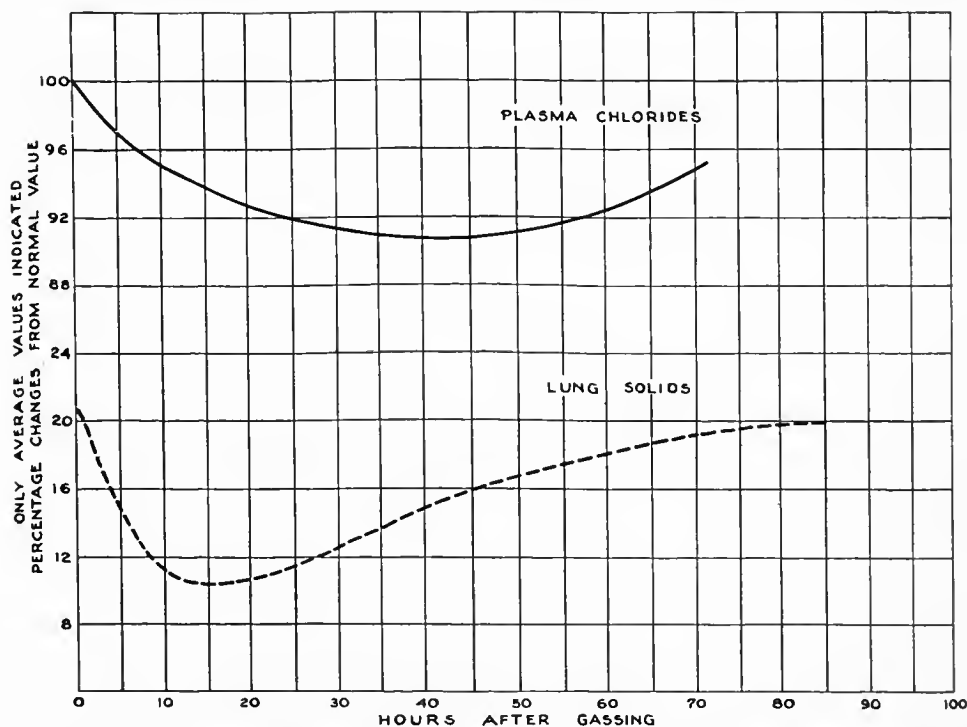


CHART XVI.—Relation between the changes of plasma chlorides and lung solids after phosgene gassing

showed a rapid increase in the chloride content following gassing (Chart XVII). There was a latent period in this inflow of chlorides extending over the first three or four hours, followed by a very rapid increase. Maximum values were obtained by the tenth hour and were maintained during the rest of the first day following gassing. After this period the chlorides left the lung and the chloride content gradually returned to normal. Complete data are not available, but the process of chloride disappearance from the lung was well advanced by the fiftieth hour and the normal was regained soon after.

From these results it becomes evident that the entrance of chlorides into the lungs determines the blood values. The amount of blood chlorides (Chart XVI) was unaltered until retention developed in the lungs. Following the

development of this lung condition the blood chlorides dropped to a minimal value and were so maintained until the fiftieth hour when a return to normal commenced. This corresponded to the passage of the acute pulmonary condition.

In animals dying from acute edema and autopsied immediately, samples of the pulmonary exudate were obtained by removal of the entire lungs and collection of uncontaminated fluid as it ran from the trachea. The fluid collected in this way was clear, straw colored, and occasionally contained a few erythrocytes. It clotted on standing. Determination of the chloride content of this fluid showed essentially the same value obtained from a simultaneous sample of blood plasma. (Table 25.) This indicated that there was

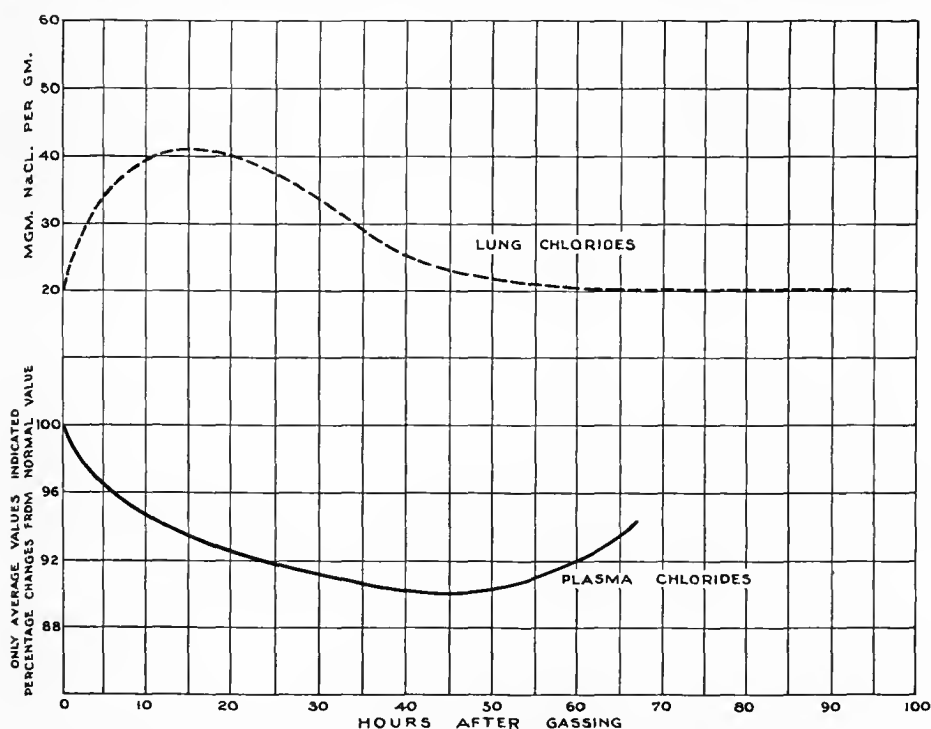


CHART XVII.—Changes in the chlorides of lung tissues and blood plasma after phosgene gassing

complete permeability of the lung capillaries for salts and that the pulmonary exudate and blood plasma were in complete equilibrium with reference to their salt content even if not exactly identical in composition.

TABLE 25.—Chloride content of blood plasma and pulmonary exudate after phosgene gassing

Dog No.	Concen- tration	Time of death (hours after exposure)	Blood plasma (mgm. NaCl per c. c.)	Pulmonary exudate (mgm. NaCl per c. c.)
124.....	67	12	5.86	5.86
461.....	70	9.5	6.72	7.25
395.....	79	31	6.68	6.75
140.....	88	22.5	6.37	6.40
257.....	93	30	5.50	5.31
Average.....			6.22	6.31

The relationship between the blood and urine chlorides was not entirely clear. The high urinary excretion of chloride during the fourth to seventh hour after gassing showed no direct connection with either the blood or pulmonary changes. During the period of chloride retention in the lung and of low blood content the urine chlorides were well below normal and only increased on the third day after gassing, when the chlorides in the lung were liberated and the blood content again rose above the threshold of kidney excretion.

EDEMA AND CHLORIDES OF TISSUES OTHER THAN THE LUNGS

With phosgene and chloropicrin the data available were too incomplete to warrant a decisive inference relative to the part played by tissue chlorides in the production of pulmonary edema. Hence these data are not included in the present discussion. With chlorine gassing, however, the liver, and to a smaller extent the muscles, showed a distinct tendency toward a decrease in the chloride content from 4 to 10 hours after gassing followed by a return to normal between 30 and 40 hours later. The change in the H_2O content of the liver was less marked than the chloride content, but the two changes tended to be parallel. It is realized that the evidence presented on this point is not entirely conclusive and it is included merely for the purpose of indicating the probable transport of chloride and fluid from the tissues to the blood.

EDEMA AND TOTAL SOLIDS OF TISSUES OTHER THAN THE LUNGS

A satisfactory explanation for the concentration of the blood during the production of edema is difficult. At least two hypotheses may be formulated: (a) Fluid is taken from the tissues to a maximum degree by the blood, whence it localizes in the lungs, the final blood concentration being caused by the inability of the tissues to supply further fluid demands made upon them by the blood. It is conceivable that extraction of fluid from a tissue, like muscle, can proceed to a limited extent only if normal processes are to obtain. (b) The hypothesis is plausible that blood concentration is caused by mere extraction of fluid from the blood, the exit of fluid from the blood producing edema not only of the lungs but of other tissues as well. If such a view is pertinent the degree of edema in tissues other than the lungs must be slight, inasmuch as there is no visible evidence of such a condition.

Analyses were made of the total solid content of tissues of dogs gassed with chlorine, phosgene, and chloropicrin. It was obvious that in order to obtain conclusive evidence in support of either of the above hypotheses a large number of determinations had to be made, owing to the individual variation of dogs with respect to the total solid content of the tissues. The data are insufficient to draw dogmatic conclusions, but are ample to indicate that the second hypothesis, namely, that there was a general edema of the tissues, does not hold. In other words, edema was not general. On the other hand, there is evidence for the view that water was drawn *from* the muscles.

As a tentative hypothesis it may be accepted, therefore, that during the development of pulmonary edema fluid was drawn from the other tissues—perhaps specifically from muscle tissue.

EDEMA AND PERMEABILITY OF BLOOD VESSELS

A discussion of edema would be incomplete without reference to a possible change in the permeability of the blood vessels, either general or local, since in a theoretical consideration of the production of edema it is generally assumed that alterations in vascular permeability may be a significant factor.

In the experiments to be reported, dogs were infused with sodium-chloride solutions before and after gassing, and changes in blood volume were measured at short intervals after infusion. This method gave the rate of return to the normal of the augmented blood volume after infusion; in other words, the rate of disappearance of the infused fluid was determined, and an indication was obtained of the comparative permeability of the blood vessels.⁵

Considerable careful work was first done to determine the applicability of the determination of hemoglobin to the measurement of blood volume. Samples taken from ear vessels were absolutely worthless unless a clean cut was made with the lancet, resulting in a copious flow of blood which appeared without manipulation or rubbing. Into the jugular vein of normal dogs was infused physiological saline solution, at 38°, so that a volume equal to 1 per cent of the body weight was injected in approximately one minute. Samples were taken from the ear before infusion and at one minute intervals after infusion until the blood volume returned to that indicated by the hemoglobin before infusion. Two-hundredths of a cubic centimeter of blood was measured by a Sahli pipette and delivered into 6 cubic centimeters of weak ammonia water. Coal gas was then passed through until the hemoglobin was changed to CO-hemoglobin, when the color was compared to a standard 1 per cent solution of CO-hemoglobin in an Autenrieth colorimeter.

With gassed dogs the procedure was the same with the exception that blood to the extent of 1 per cent of the body weight was withdrawn one hour after gassing, as in the standard treatment.^d The infusion was made five hours after gassing, when the blood usually had concentrated above normal. A comparison of the time for the blood volume to return to normal after infusion in the normal dog with the corresponding time in the gassed dog, gave an indication of comparative permeability.

The results obtained were definite. The time for the infusion fluid to disappear varied from 0 to 21 minutes in normal dogs and from 8 to 33 minutes in gassed dogs. In all dogs save one, the time for the infusion fluid to disappear was longer after gassing than in the normal dog. The time for infusion fluid to disappear in normal dogs varied; i. e., it was an individual characteristic and the decrease in permeability after gassing likewise varied with different dogs. It should be emphasized that there was no evidence of increased permeability, with a single exception, and a very definite indication that the permeability of the vessels was somewhat decreased during the stage of phosgene poisoning studied.

From the foregoing considerations it may be accepted that the development of edema as a result of the action of the lethal war gases was associated with well-defined changes in the fluid and salt content of the blood and tissues without an apparent increase in the permeability of the blood vessels. Fluid and salt probably passed from the tissues to the blood in an attempt to com-

^d This was done for a purpose having no connection with the present investigation and does not militate against the conclusions drawn, inasmuch as this procedure did not noticeably change the development of edema.

pensate the latter for its loss in those constituents which mobilize in the lungs, resulting in edema. Later, if edema subsided, there might be reabsorption of fluid and salt, a portion being redistributed to the tissues, the remainder being excreted through the kidneys. Such a hypothesis was supported by the correlation existing between the production and subsidence of edema, and the excretion of chlorides through the urine previously discussed.

OXYGEN CHANGES IN THE BLOOD

From the fact that the lethal war gases exert a specific action upon the respiratory mechanism leading to impairment of the mechanism of respiration, it is obvious that distinct changes in the respiratory function of the blood are to be anticipated. This view is corroborated by the superficial observation that the blood changed in both its consistency and color. It became viscid and thick, and instead of possessing the normal bright red hue might assume a maroon color, often appearing almost black.

The subject of the respiratory function of the blood is of extreme importance, since upon its proper performance depends adequate tissue nutrition and continued existence of the organism as a whole. Oxygen starvation is an exceedingly serious condition resulting in impairment of all bodily functions, and if sufficiently grave, culminating in cessation of all vital activity.

OXYGEN CAPACITY OF THE BLOOD^e

By the oxygen capacity of blood is meant the cubic centimeters of oxygen in 100 cubic centimeters of blood which has been thoroughly aerated with atmospheric air at room temperature. Obviously the oxygen capacity of the blood is a measure of the hemoglobin present. From comparative studies of the total solids of the blood and oxygen capacity it appears that variations in oxygen capacity and hemoglobin can be accounted for by variations in the concentration of the blood by the lethal war gases.

With phosgene poisoning there were three distinct periods of fluctuation of the oxygen capacity. First, in all but a few dogs there was a diminution of the oxygen capacity immediately after gassing which lasted from four to seven hours. Secondly, there was an increase of the oxygen capacity which, in dogs that died, reached a maximum between eight and twelve hours, but in dogs that lived this value reached a maximum later. The third period marked a decrease in the oxygen capacity to normal which was reached at the twenty-fourth to thirtieth hour after gassing. The value for oxygen capacity sometimes fell to a figure slightly below normal during this later period. The above picture was the usual one to which by far the largest number of animals conformed. Occasionally, there was observed a case in which there was no diminution of oxygen capacity immediately after gassing, but instead a rapid increase to a maximum. Such animals usually died. Occasionally, also, an animal was observed whose oxygen capacity did not change at all, but fluctuated about the normal, during the entire period of observation. These animals usually lived. All of these oxygen capacity figures were paralleled by total solids figures so that it seemed justifiable to assume that one was not dealing with newly intruded corpuscles, but only with changes in the concentration of the blood. The oxygen capacity was determined in both venous and arterial blood, the values being the same in both cases.

^e The methods of Haldane and Barcroft were employed in the determination of changes in the gases of the blood.

The picture with reference to oxygen capacity was as follows: An immediate decrease, a subsequent increase to a maximum, followed by a return to normal or subnormal. These changes were independent of the concentration of gas to which the animal was exposed.

Immediately (up to one hour) after gassing with chloropicrin the oxygen capacity fell down markedly in 17 animals, slightly in 5, did not change in 2, rose slightly in 2, and markedly in 3. Treated statistically, this evidence indicates that there was a dilution of the blood in a majority of animals immediately after gassing with chloropicrin.

This first period of lowered oxygen capacity was brief (much shorter than the corresponding period in phosgene poisoning) and lasted less than two or three hours. Occasionally, this lowered oxygen capacity persisted in an animal for more than 24 hours. Two such animals in these experiments survived low concentrations of gas.

It is noteworthy that 12 of the 13 animals that died showed lowered oxygen capacity immediately after gassing. At low concentrations about one-half of the animals that showed this marked drop in oxygen capacity succumbed to gas poisoning. Of the eight deaths at high concentrations, seven showed diminished oxygen capacity immediately after gassing.

Following the initial short period of diminished oxygen capacity there was a quick rise above the normal figure. This reached its maximum between the twelfth and sixteenth hours in animals that survived. The maximum might come as early as the fourth hour and as late as the twenty-fourth. In dogs that died the maximum usually was found at the time of death. At high concentrations of gassing this maximum seemed to come rather early (4 to 10 hours). Finally, there was a third period in surviving animals when the oxygen capacity dropped to the normal or slightly below normal in 24 to 48 hours.

Briefly, then, the picture with reference to oxygen capacity was as follows: (1) An immediate decrease lasting only an hour or two; (2) a subsequent increase to maximum at death or 12 to 16 hours; (3) a slow decrease to normal or subnormal.

A study of the blood of dogs gassed with chlorine demonstrated that after gassing there was always a significant rise in the oxygen capacity.

OXYGEN CONTENT OF ARTERIAL BLOOD

By oxygen content is meant the cubic centimeters of oxygen in 100 cubic centimeters of blood just as it is drawn from the animal. The blood was drawn under oil to prevent contact with air, and in all the manipulation incident to the analysis contact with air was carefully avoided.

In the first period after gassing with phosgene in all dogs the oxygen content in arterial blood dropped slightly. In the second period the oxygen content tended to rise somewhat above normal in dogs that lived, while in dogs that died it rose slightly, then decreased steadily until death, when the value might be as low as one-half that of normal blood. In the third period in dogs that lived the oxygen content fell back to normal or slightly below.

The oxygen content may also be expressed in percentage of the capacity, which value is known as the percentage saturation. Expressed as such, the percentage saturation in the first period was within normal limits. In the second period the percentage saturation was often within normal limits at

first, but toward the last of this period and during the third period the percentage saturation would fall to a point slightly below normal in dogs that lived. In dogs that died the percentage saturation began to fall during the second period and at death was as low as one-half of the normal.

To summarize, the oxygen content of arterial blood taken as such did not vary greatly after gassing in dogs that lived. When taken together with the increase in oxygen capacity, however, it is apparent that the percentage saturation of arterial blood was reduced after gassing.

In the first period after gassing with chloropierin the oxygen content of the blood dropped somewhat in 19 dogs. It rose above normal in 6 dogs, and did not change in 4. This drop occurred in 90 per cent of the dogs gassed at high concentrations, while at low concentrations only 60 per cent showed this initial drop. In animals that died the arterial content of oxygen usually dropped as death approached. In the second period (i. e., after three or four hours from gassing) the arterial oxygen content tended to rise to a maximum, which appeared sometime between 8 and 24 hours. In the final period, the arterial oxygen content diminished, often to subnormal values.

In the period immediately after gassing the percentage saturation of oxygen was within normal limits. It rose or fell in a manner somewhat parallel to the oxygen content discussed above. In 12 animals the percentage saturation rose above the normal. In the period following the percentage saturation of the arterial blood usually dropped steadily for animals that died. In animals that survived the percentage saturation did not go below 70. The lowest figure was reached usually between 12 and 18 hours. After that it rose again to normal in 24 to 48 hours.

To summarize, the oxygen content of arterial blood taken as such did not vary enough in surviving gassed dogs to be appreciably significant. In dogs that succumbed the lowered arterial oxygen content was closely paralleled by the increasing weakness of the animal. The arterial oxygen saturation was actually increased immediately after gassing in a number of animals (12 out of 29)—mostly in those that died. No determinations were made with chlorine relative to the oxygen content of arterial blood.

THE OXYGEN CONTENT OF VENOUS BLOOD

In dogs that lived the value for oxygen content of venous blood after phosgene gassing dropped slightly immediately after gassing and thereafter fluctuated about a value which was below normal. In dogs that died, however, after the first decrease the value continued to drop rapidly until death, where the value for oxygen content in venous blood was often reduced to almost zero. Expressed as the percentage saturation, the value for venous blood was within normal limits during the first period, but dropped to a lower level in periods two and three in dogs that lived, while in dogs that died the percentage saturation fell during the second period to a value that sometimes was only one-fourth the normal.

The oxygen content of the venous blood after chloropierin gassing dropped immediately after gassing in nearly all animals. In those that lived, the drop was on an average the same as in those that died. This average value was between 50 and 60 per cent of the normal, regardless of the concentration of gas used. In the great majority of surviving animals, the venous oxygen content

did not return to normal in 48 hours. On the contrary, the value, though steadily increasing after the initial heavy drop due to gassing, remained usually at a low level for at least 48 hours. The percentage saturation of the venous blood presented essentially the same picture as described above for the venous oxygen content.

In a general way, then, the blood oxygen picture in chloropierin poisoning was roughly similar to that found after phosgene gassing. If it is assumed that a drop in oxygen capacity is due to blood dilution and vice versa, it is found that a majority (22 out of 29) of the animals studied here showed blood dilution immediately after gassing with chloropierin. The main difference in the initial dilution phases in phosgene and chloropierin poisoning was in the duration of dilution. With chloropierin it would last two or three hours, while with phosgene it was about six to eight hours long. The concentration of blood then followed in both types of poisoning. With chlorine gassing the oxygen content of venous blood usually showed a marked decrease which could be maintained for many hours.

DISCUSSION OF ALL OXYGEN DATA

From the data presented it is quite apparent that the changes in arterial blood must be intimately associated with alterations in blood concentration. In all three instances the change in oxygen capacity and arterial content closely approximated the corresponding fluctuations in blood concentration. With phosgene and chloropierin the general character of changes under discussion was of the same kind, the difference being in the time relationships. The chlorine data differed in character from those of phosgene and chloropierin in that with chlorine there was no initial drop in the oxygen capacity or arterial content. Instead there was an immediate progressive rise. A graph representing the general changes in phosgene is shown in Chart XVIII. The corresponding chloropierin curve was so similar that it is omitted.

From the foregoing it may be concluded that changes in blood concentration adequately account for the observed alterations in oxygen capacity and arterial oxygen content. With phosgene and chloropierin there was a corresponding initial fall synchronous with the dilution of the first period and a marked rise coincident with the increase in blood concentration. The rise in oxygen capacity and oxygen in arterial blood with chlorine corresponded with the changes in blood concentration.

When oxygen in the venous blood is considered, the changes observed with the three gases do not yield so simply to interpretation. It is true that the initial drop and the first rise in oxygen content corresponded with changes in blood concentration. The mechanism whereby this was brought about may involve several factors. Some of the factors which need consideration are edematous fluid in the lungs, circulation rate, concentration of the blood. It has been asserted that in the presence of lung edema a film of water forms over the pulmonary capillaries, through which oxygen must pass in addition to the capillary wall. This would result in the blood in the pulmonary veins being deficient in oxygen. The arterial blood, then, with an abnormally high value of oxygen capacity, does not have a corresponding high value for oxygen content, with the result that the percentage saturation drops in the arterial blood after the lung edema becomes well developed: that is, in the second period

and the first part of the third period. Other conditions remaining constant, such a state would result in the tissues being supplied with oxygen by blood subnormally saturated with oxygen and could lead to a drop in the content of venous oxygen.

This explanation, however, will not adequately account for the gradual continued fall in venous oxygen, nor do other conditions remain constant. The blood continues to concentrate to a point where its passage through capillaries must become greatly impeded by the increased viscosity of the circulating fluid. In other words, the blood remains longer than usual in contact with the tissues and hence is robbed of an unusual quantity of oxygen. The continued increase in concentration ultimately reacts further upon the heart efficiency, less blood than usual being circulated in a given period, and even

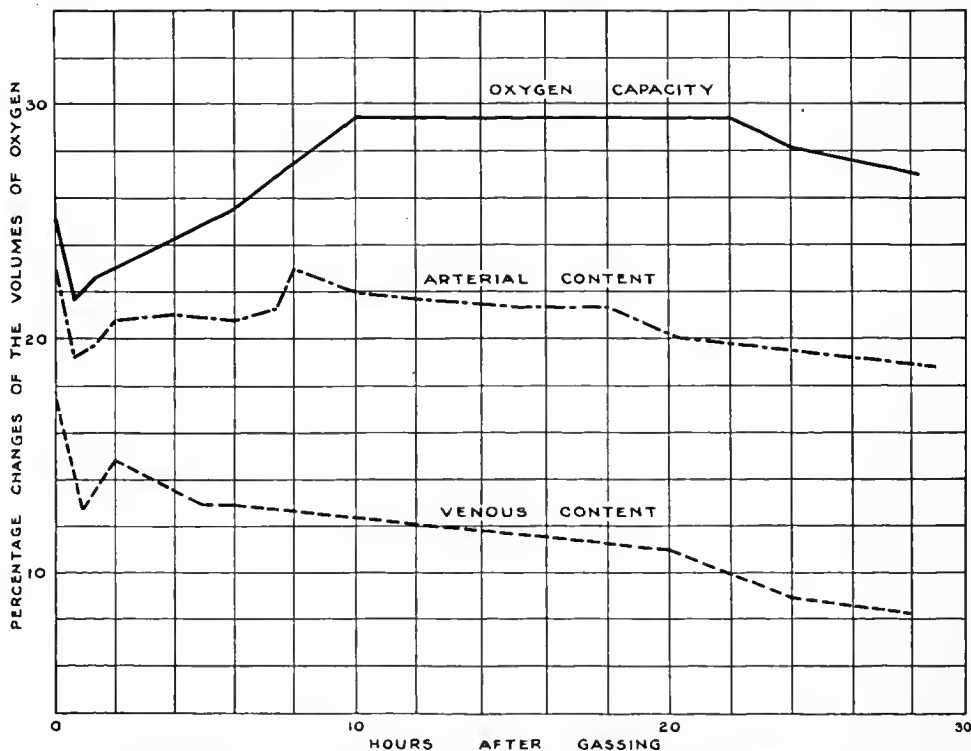


CHART XVIII.—General changes in the oxygen capacity and content after phosgene gassing

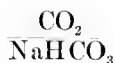
though the oxygen content of this blood may be abnormally high there is finally an insufficient oxygen supply carried to the tissues. In other words, the concentration of the blood causes a circulatory failure which becomes progressively worse as blood concentration increases and the oxygen of venous blood becomes progressively low. Under these conditions the tissues must suffer from lack of oxygen and the nervous mechanisms tend to assume a condition of narcosis.

The effect of oxygen want upon the heart will be to destroy its efficiency, the concentration and contracting force are decreased, and the heart may pass into a state of dilatation. As an accompaniment to the changes outlined

above, the blood pressure may fall markedly and the animal pass into a condition greatly resembling shock. The final analysis of the changes of oxygen in the blood leads back to the alterations of blood concentration as the primary cause.

ACIDOSIS

The condition resembling shock exhibited by animals after chlorine poisoning led to the study of acidosis. This was taken up by investigating the urine, the bicarbonate content of the blood, and the hydrogen ion concentration of the blood. The nature of the carbon dioxide—bicarbonate equilibrium in the plasma makes the sodium bicarbonate assume the rôle of a respiratory compound. Alkali or rather sodium ions are constantly being drawn from the tissue reservoirs to hold carbon dioxide in the blood and also constantly pass into the tissue reservoirs when the carbon dioxide tension in the blood is less. In other words, there is a considerable "alkaline reserve" in the animal body. An abnormal appearance of acid in the body leads to a reduction of this reserve. Hence the measurement of this sodium bicarbonate concentration in the blood gives an index to the reaction of the body; i. e., to the maintenance of the proper alkalinity or of an acidosis. The method of Van Slyke and Cullen was used. The blood was drawn without loss of carbon dioxide. The equilibrium



was established at room temperature and at the tension of carbon dioxide in alveolar air.

The results with gassed dogs led to the conclusion that all animals gassed with chlorine showed an immediate acidosis (lowered alkali reserve) of more or less severity. This lowering of the bicarbonate content of the blood was an invariable result of gassing and though the degree of this acidosis was extremely variable, it carried no relationship to the concentration of chlorine to which the animal was exposed. Some interesting correlations between the ability of the animal to withstand the acute stage of chlorine poisoning and the bicarbonate value were observed. When the value fell from the normal, which ranges from 50 to 70, to below 40, the animal usually did not survive. Not all animals whose bicarbonate value rose after the first drop recovered; but all animals which survived the acute period had bicarbonate values rising sharply after the first drop. Again, in animals which were gassed more than once there seemed to be an overcompensation for the loss of alkali for each time the normal was higher than that before the previous gassing. This same sudden drop in the bicarbonate value was also observed when the concentration of the gas was very low. This loss of bicarbonate could be made good to the animal by intravenous injection or per os administration of sodium bicarbonate.

The causes of this acidosis are at best obscure. There are two theories each of which has its good points. There are certain facts which point to the absorption of chlorine as the cause for the acidosis. The fact that there was an immediate lowering of the bicarbonate value points to a cause which operated immediately and which was not cumulative. This appeared to be entirely independent of the concentration of the gas to which the animal was exposed. It was demonstrated that direct chlorine absorption probably did

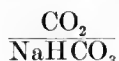
not account for the observed changes in the tissue and blood. On the other hand, in the experiments on the bicarbonate value of the blood the amount of chlorine calculated to be necessary to produce the observed acidosis was exceedingly small—too small, in fact, to be determined by the most refined methods of analysis. Again, in the urine sometimes there was observed an immediate, though not large, increase in hydrogen ion concentration and usually in titratable acidity. These facts lead one to postulate a cause which is instantaneous in its action. The objection to the theory that the acidosis was due to the absorption of chlorine is found in the absolute lack of all correlation between the concentration of chlorine in the mixture breathed by the dog and the degree of acidosis produced. Since it was demonstrated that the musculature of the bronchioles contracted when the chlorine came in contact with it, this may account for the inability of the chlorine to penetrate into the alveoli and hence for the independence of the chlorine concentration and the loss of alkali.

The second theory is that of a carbon dioxide acidosis. When the chlorine struck the lung tissue more or less irritation, with the accompanying edema, resulted. This edema and the excessive secretion of mucus along the nasopharyngeal passages and trachea were always well developed at the end of the half hour gassing period. Along with this edema, as a result of the chlorine irritation, appeared the contraction of the muscles of the bronchioles. With the air passages contracted and the alveoli filling with edema fluid, the lung rapidly became seriously impaired for the purpose of allowing a free passage of oxygen into, and of carbon dioxide out of, the blood stream. This accumulation of the carbon dioxide in the blood, as the result of the inability of the carbon dioxide to leave the blood in the lung, if followed to its conclusion, would merely result in a readjustment of the ratio



by calling forth more alkali from the tissue reservoirs. This was exactly what happened after some five or six hours in dogs which had a fund of alkali to draw upon. In the meantime, however, there was a rapidly increasing tension of carbon dioxide in the blood without a compensating increase in alkali, and the result was a carbon dioxide acidosis. This condition would account both for the immediate moderate increase in the acidity in the urine after chlorine gassing, and for the high bicarbonate value in dogs which lived for 24 hours. Since the high bicarbonate level means merely a compensating mechanism and not the removal of the cause of the pathological condition, one can understand the reason for the fact that not all animals survived whose bicarbonate level returned to normal or above.

The objections to the above interpretation are that it has not been possible to demonstrate in any case an increased content of carbon dioxide in venous blood after gassing, while it may be shown that the ratio



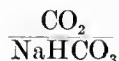
was adjusted in considerably less time than the theory demands. Still another possible explanation of the acidosis is the insufficient oxidation which results

from aeration of the blood, the acid products of metabolism producing the characteristic acidosis. It is obvious, however, that the data at hand are insufficient to offer at present a final solution of the acidosis problem, but it is probable that acidosis will prove to be a resultant of the operation of all three factors discussed.

THE HYDROGEN ION CONCENTRATION OF THE BLOOD

In addition to the determination of the acidity of the urine and the bicarbonate in the blood the hydrogen ion concentration of the blood is available as an indication of acidosis. The P_H of blood is normally 7.4, which means that there is a slight preponderance of hydroxyl ions. The "buffer" value of blood is high and it is only in extreme acidosis that the reaction, as shown by the hydrogen ion concentration, changes, hence a study of this factor gives us valuable data on the degree of acidosis. The method of Levy, Rowntree, and Marriott was used. The whole blood was dialyzed against a neutral physiologic saline solution and the P_H of the dialysate measured.

Whereas the P_H of normal blood is 7.4, after gassing the value fell to 7.3 and 7.25. When the air was blown through the dialysate the value went up to 8.2 in all cases. Although the drop from 7.4 to 7.25 was small numerically, in view of the high "buffer" value of the blood and the well-known fact that it is the last tissue to change in its chemical characteristics, the observed values indicated a severe upset of the acid-base equilibrium. In the dialysate all of the salts in the blood were present, including sodium bicarbonate and ionized carbonic acid, so that there was the same ratio



in the dialysate as in the blood. If, after dialyzing, the carbon dioxide was blown out with air, the base formerly held as bicarbonate appeared as the more alkaline bicarbonate. If, however, the acidosis was due to fixed acids, the blowing out did not affect the hydrogen ion concentration; at least not to the extent observed. The fact that in every case the blowing out reduced the hydrogen ion concentration to the same value, 8.2, indicates strongly that the acidosis was caused by carbon dioxide rather than by fixed acids.

In brief, the blood picture after chlorine gassing was, on the basis of the data presented, as follows: The chlorine irritated the lung tissue, causing the bronchiolar musculature to contract and also edema to appear. As a result of the edema the blood became concentrated. The curtailed aeration, resulting from the edema, the concentrated blood, and the bronchiolar muscle contraction, resulted in a low degree of oxygenation of the blood; it resulted also in the inability to get rid of the carbon dioxide with the consequent accumulation which gave rise to a temporarily diminished alkaline reserve and to an increased hydrogen ion concentration. The decreased rate of circulation resulted indirectly in a very low carbon dioxide content of the venous blood. These altered conditions tended to return to normal in 24 hours.

The acid-base equilibrium in the blood was distinctly affected by gassing with phosgene, but in no definite direction. Whereas with chlorine there was invariably a drop in the bicarbonate value immediately after gassing, with phosgene the bicarbonate value dropped in some cases and increased in other

cases. In a normal animal the bicarbonate value is constant, never varying more than two or three volumes per cent. In dogs gassed with phosgene the variations above and below normal were large, sometimes as much as 10 volumes per cent. There was one definite tendency, however, and that was the drop in bicarbonate value as the animal approached death. This terminal acidosis was observed in all animals that died 10 or more hours after gassing. The P_H value varied only slightly with the change in bicarbonate, the final drop as the animal approached death being the only pronounced change.

It may be concluded, then, that although phosgene caused a wide fluctuation in the bicarbonate value, there was no definite acidosis until the terminal stages. These appearances of acidosis must be referred, therefore, to the consequences of oxygen want in the terminal stages of phosgene poisoning and can not be regarded as a specific action of the gas.

With chloropierin there seemed to be no marked effect of the gassing until some eight hours after gassing. During the first eight hours the values fluctuated about the normal. The P_H determinations varied, in most cases, with the bicarbonate value. After the 8-hour period there was a gradual decline in both values, probably indicating an acidosis condition, though in neither case did the animal die within 24 hours. It appears, then, from the scant data on hand, that there was no immediate acidosis following poisoning by the lethal doses of chloropierin.

It may be concluded, therefore, that the lethal gases fall into two groups with respect to the production of acidosis. With chlorine there was evidence of an immediate carbon dioxide acidosis which later may become readjusted, whereas with phosgene and chloropierin, acidosis was apparent only in the terminal stages of poisoning and can hardly be accepted as being a specific response of the action of the gases. It is much more reasonable to regard this acidosis as a terminal acidosis induced by the condition, general depression, of the animal.

AN INTERPRETATION OF GAS POISONING

In the preceding pages an outline has been given of the changes that occurred in the organism as the result of exposure to the lethal gases. Re-stated briefly, the gassing had a definite influence upon respiration, pulse, temperature, blood concentration; water content of the lungs and tissues; chloride content of blood and tissues, with resulting changes in chloride excretion by way of the kidneys; red and white cells and hemoglobin of the blood; distinct alterations in oxygen of the blood, leading to dyspnea and partial asphyxia; the presence of acidosis at times, and a definite influence upon protein metabolism.

The effects of gassing as thus enumerated are so various and devious that an attempt toward correlation or the assignment of cause and effects seems at first glance well-nigh impossible. Further inspection of the data presented, however, brings to light one significant feature which stands out clear and distinct from all other effects induced by exposure to gas. This is the well-defined curve of changes in blood concentration. Upon the basis of alterations in blood concentration quite definite stages in gas poisoning may be outlined. These stages stand out most clearly with phosgene and; therefore, the picture presented by this gas will be considered first.

STAGES IN PHOSGENE POISONING

First stage.—In the first few hours (five to eight) after phosgene poisoning there was a notable decrease in the concentration of the blood. The decreased concentration occurred rapidly and then the blood gradually assumed the normal concentration. In this period there was sometimes a significant dilatation of the heart (observed by Eyster). Accompanying the decreased concentration of the blood there was a sharp drop in the chlorides of the blood and a marked increase in the chlorides and water content of the lungs. The chlorides of the urine increased immediately after gassing, reaching a maximum between the third and seventh hours, then decreasing. The heart beat was distinctly slowed at first, with a tendency to regain the normal or be somewhat above normal before this period was over. The immediate effect upon the respiration was a distinct increase in the rate. During this period the temperature showed a marked increase, attaining a maximum coincident with the termination of this period. Oxygen capacity, erythrocytes and hemoglobin followed a curve parallel with that of the changes in the concentration of the blood throughout all stages of phosgene poisoning. Oxygen content of both arterial and venous blood decreased significantly. The saturation of hemoglobin with oxygen decreased somewhat. In general, the decrease was more marked in the venous than in the arterial blood. In the first period an influence upon protein metabolism was not noticeable.

Second stage.—The period (five to eight hours) of blood dilution was followed by an interval during which the blood rapidly became concentrated to a point far beyond the normal value and remained near this level for several hours. In this stage the heart could be markedly decreased in size (Eyster). During the period of increased blood concentration the chlorides of the blood showed a tendency to regain the normal. The water and chlorine content of the lungs reached a maximum and then gradually decreased. The urinary chloride excretion was normal or subnormal. The heartbeat and respiration were both markedly accelerated.^f The temperature, on the other hand, steadily decreased to a degree or more below normal. If the animal died in this stage the temperature might fall steadily up to the time of death. Most of the fatalities occurred in this stage. The oxygen content of arterial blood remained fairly stationary at a nearly normal value, whereas that of venous blood fell rapidly to a very low level. The saturation of hemoglobin with oxygen decreased rapidly in both arterial and venous blood, but the fall was greater in venous blood. There was no evidence of an influence upon protein metabolism.

Third stage.—After the period of increased concentration the blood gradually became more dilute until it was slightly under the normal value, which was eventually gained, and the animal recovered. The chlorides of the blood gradually regained the normal level. The chloride and water contents of the lungs followed a similar course. In animals reaching this stage the heart beat and respiration rose to a maximum and then gradually attained the normal. The temperature rose to normal or above in animals that eventually recovered. In animals that died during this period the heartbeat and respiration increased, but the temperature steadily fell. The oxygen content of

^f In animals that were in a serious condition, although the rate of respiration was markedly increasing, there was a decrease in depth, so that rapid shallow breathing existed.

arterial and venous blood tended to regain the normal. Chloride excretion by the kidney was markedly decreased, but later was much augmented. Coincident with the increased chloride excretion was a noticeable increase in the protein metabolism.

The interpretation which may be placed upon the different stages of phosgene poisoning is as follows: In the first stage there was a marked dilution of the blood. There are at least two ways in which this dilution may be explained. In the first place, it may mean an increased blood volume, the excess fluid finding its way into the blood from the tissues in response to the strong irritative stimulus exerted by the gas upon the respiratory tract. Or, secondly, a diluted blood would result if the red cells were removed in part and deposited in some organ or tissue. In these investigations no studies were made to determine actual changes in blood volume. Reports by Eyster and Meek,⁴ however, who made such estimations, tend to the conclusion that in the stage under discussion blood volume is not increased, and they account for the dilution of the blood on the hypothesis that red cells are stored in the lungs, at least temporarily. Whichever explanation is correct, it is certain that during the first stage two features may be quite prominent, namely, edema of the lungs and dilatation of the heart. Edema may be explained very readily on the hypothesis of increased blood volume, and it is possible also that such a condition might lead to a dilated heart. On the other hand, the deposition of corpuscles in the lungs by causing an obstruction in the circulation would lead to a dilated right heart. The relatively large transport of fluid to the lungs during this period, however, is not explained so easily by this hypothesis. Whichever hypothesis is accepted, edema of the lungs prevails, and there may be a dilated right heart.

In the second period edema has reached its maximum development, and here also blood concentration is at its height. The latter state is undoubtedly induced by the withdrawal of fluid which finds its way into the lungs. During the interval of blood concentration the blood volume is definitely decreased and the heart may be noticeably diminished in size (Eyster). This would presumably result in a decreased efficiency of this organ and would lead to an inadequate circulation. Later, when the blood resumes its normal degree of concentration, normal heart action is reestablished.

The development of edema induces a mobilization of chlorides in the lungs at the expense of the chlorides of the blood, the lowered chloride content of which may also be explained in part by loss of chlorides through the kidneys, since at this period the output of chlorides in the urine is appreciably augmented. Later during the second period, the chlorides of the lungs reach a maximum, the blood content is not called upon and, therefore, an approximately normal blood chloride content may be found which is maintained thereafter. This chloride retention by the lungs coincides with the fact that on the second day of phosgene poisoning the urinary excretion of chlorides is usually below normal. The period of readjustment now follows during which edema subsides in the lungs, and presumably both fluid and chlorides are demobilized by the lungs and find their way into the blood. The excess of chlorides over the normal in the blood is eliminated through the kidneys, which would account for the large output on the third day after gassing.

The changes in oxygen capacity, erythrocytes, and hemoglobin followed the curve of alterations in blood concentration throughout the entire course of phosgene poisoning, which might well be anticipated. Oxygen content of arterial blood in general showed relatively unimportant changes, whereas that of venous blood progressively diminished throughout the first and second periods of phosgene poisoning. This may be explained in the first period by the fact of diluted blood and in the second period was undoubtedly caused by the longer contact of the blood with the tissues, induced by an inefficient circulation.

The respiratory changes were correlated with the impaired respiratory functions of the blood, such as lowered inhibition. The later rapid pulse was directly induced by the viscous character of the blood which caused oxygen want. Although specific data are lacking, it appears quite evident that there was distinct fall of blood pressure. One may assume a direct relationship between the heart's efficiency and temperature. Thus, in the first part of the first period the heart action was slow, there was inefficient circulation, and the temperature fell. Later, the greatly accelerated pulse was accompanied by a rise in temperature far above the normal. From this it would appear possible that the heart had temporarily overcompensated, resulting in an efficiency of the circulation above the normal level.

Now follows the period of concentration of the blood. This concentrated blood is, without doubt, more difficult to circulate through the body, and if the heart is doing only its normal work there will be, as a result of the thickened blood, a circulation of less than normal efficiency and such a condition apparently results in a falling temperature. In case the heart responds with a much higher rate during the period of concentration, so that even with the thickened blood it appears that a circulation of close to normal efficiency is being maintained, it will be found that the temperature is also well maintained.

In the animals which were less seriously affected and in which only a slight edema of the lungs developed, with a consequent slight loss of fluid from the blood, it was found that the temperature was well maintained provided the heart rate was normal. However, even in such cases the continuous, though slight, loss of fluid from the blood would eventually result in a concentration of the blood which would bring the circulation below normal efficiency, even with a high pulse rate, and the temperature would slowly drop until at about the twenty-fourth hour it was about 1° C., below normal. On the other hand, in the animals which were seriously affected, the blood concentrated very rapidly. The heart, even though the rate was maintained far above normal, was nevertheless not able apparently to maintain a circulation of normal efficiency, the temperature dropped very rapidly, and the animal died within less than 24 hours after gassing. In brief, then, it seems plausible that the temperature is directly related to the efficiency of the circulation and this in turn is determined, in part at least, by the concentration of the blood and the pulse rate.

This view appears to be further strengthened by the results obtained from the study of animals gassed with chloropicrin and chlorine. In both of these cases there was, in general, a state of concentration of the blood beginning immediately after gassing. Only in rare instances did a dilution of the blood occur and then it was only for a short time. From the first, then, in animals poisoned with these gases there obtained a condition in which the blood was

above normal in concentration and in correspondence with this the temperature remained below normal and the more seriously the animal was affected and the greater the concentration of the blood, the greater was the fall in temperature.

Phosgene poisoning has been considered in detail since it is unique in showing among its effects the initial period of blood dilution. At times chloropicrin presented a similar stage, but this interval was never so pronounced either in degree or length as obtained in phosgene poisoning. Usually a preliminary dilution period was lacking. It is this period that undoubtedly gives to phosgene the distinction of possessing a so-called "delayed action." Chlorine gas rarely, if ever, caused a period of blood dilution. In general, if one should consider the changes in blood concentration outlined for phosgene minus the initial dilution period, the remaining curve would represent fairly accurately the alterations occurring in the blood in both chlorine and chloropicrin poisoning. This would, of course, entail differences in time relationships, but under the conditions noted the changes in blood concentration of chlorine and chloropicrin would be accompanied by the same general type of effects which are obtained with phosgene. Under these circumstances it appears superfluous to recite further the correlation of the effects of chlorine and chloropicrin poisoning.

THE CAUSE OF DEATH IN GAS POISONING

It is generally assumed that death, in gas poisoning, is due directly to edema of the lungs, aided, of course, by the accompanying congestion. It has been said that death is caused by an individual literally drowning in the water of his lungs. The quantity of water present may reach as high a figure as a liter or more and such a conception of the cause of death seems quite obvious. On the other hand, one may well ponder whether death is usually induced in this way or whether there may be some other cause to which one may point with more certainty. The most obvious condition, other than edema, which could lead to death is the concentration of the blood. Of course, it is evident that edema and blood concentration are closely associated. Edema is assuredly the cause for blood concentration and thus indirectly, at least, brings about death, but it would appear that blood concentration is much more likely to produce death than is the presence of fluid in the lungs. There are, therefore, two possibilities open.

Death by edema could be caused by the prevention of an adequate oxygen exchange in the pulmonary blood. On the other hand, through extensive experiments of Winternitz,⁶ it is quite possible to introduce large quantities of fluid directly into the lungs of normal dogs without causing death, the fluid being absorbed with surprising rapidity. It must be conceded, however, that the conditions obtaining in the lungs of a normal dog and in those of a gassed animal are quite different, for in the experiments cited simple salt solution was introduced, whereas in an edematous lung the fluid more nearly represents blood plasma. Such a fluid would have a much greater tendency to inhibit adequate oxygen exchange than would a simple salt solution. The adherents of the idea that edema is the cause of death must ascribe death to asphyxiation. There is little doubt that well-developed edema does interfere with oxygen exchange of the pulmonary blood, but usually the efficiency of the arterial blood as an oxygen carrier is surprisingly high. It would seem a simple matter to put the question to the test experimentally. Thus, it might be assumed that if edema is the

cause of death, this operating by producing asphyxia, administration of oxygen should save the animal provided the oxygen could be absorbed. Such experiments were carried through in this investigation, and the results demonstrated that, even though the oxygen in the arterial blood may be raised and maintained in the higher normal limits, death intervenes as usual. Then, again, some animals seemed to die with much less edema than others, and the different gases also possessed different degrees of ability in provoking edema. If edema is the cause of death it is difficult to explain why some animals, with an apparent excessive quantity of fluid in the lungs, should have survived. Death is caused by something more than simple inability of the blood to absorb oxygen, by something more than a physical obstacle in the lungs.

It seems quite logical to assume that blood concentration is immediately responsible for death. Blood concentration means a failing circulation, an inefficient oxygen carrier, oxygen starvation of the tissues, fall of temperature, and finally suspension of vital activities. The whole aim of treatment was to prevent blood concentration or else restore it to the normal level. When this was accomplished the animal survived in spite of the fact that the lungs might be very edematous. It may be stated, then, that in the presence of edema and a concentrated blood, entrance of oxygen into the circulation did not prevent death. On the other hand, restoring blood to the normal concentration enabled an animal to survive even though an extensive edema existed. Administration of oxygen under the last-named conditions undoubtedly made recovery easier. Therefore, while it is accepted that indirectly the edema of gas poisoning results in death, the immediate cause of death must be assigned to blood concentration.

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CHAPTER XI

PHYSIOPATHOLOGICAL ACTION OF ACUTE PHOSGENE POISONING^a

If the effects of phosgene on the animal organism were to be described in one phase it would be by the words "pulmonary edema." A study of phosgene poisoning is, therefore, of more than passing medical interest. The work here reported was done in an attempt to get a physiological background for proposed forms of treatment. Various physiological reactions have been followed as closely as possible throughout the course of fatal phosgene poisoning.

The general results of poisoning by lung-irritant gases, including phosgene, have been described in the preceding chapter, and since the experience on this point here reported is identical, such description need not be repeated. The division of phosgene poisoning into three stages (see pp. 351-354) is in accord also with these findings and, although arbitrary in certain cases, as all such classification must be, it is of distinct advantage in locating the various physiological disturbances and in gaining an insight into the condition as a whole.

METHODS

Dogs were used throughout these studies. The animals were subjected for 30 minutes to air containing 80 to 100 parts per million of phosgene. This was sufficient, with rare exceptions, to produce death in the first 24 hours. The technique of this gas administration was one gradually evolved at the various Chemical Warfare Service laboratories. It consisted of placing the dogs in a 100-liter air-tight glass box through which air was drawn at the rate of 100 liters per minute. The phosgene cylinder was connected to the air inlet tube, the gas outflow being regulated by a needle valve and the rate roughly determined by a flowmeter. From the gassing chamber itself air was drawn in order to determine by chemical analysis the exact concentration of phosgene to which the animals were subjected.

All animals on which it was necessary to make incisions were morphinized either before or immediately after being gassed. A series of morphine controls had been carefully studied, and care was taken that none of the effects to be described could be attributed to morphine. In order to make observations rapidly and frequently, the animals were kept tied to operating boards. Since no pressure was exerted anywhere except by the cords on the limbs, and the respiratory passages were entirely unobstructed, this restraint seemed unobjectionable. The animals lay quietly and comfortably until the usual asphyxial stimulations occurred shortly before death.

ARTERIAL BLOOD PRESSURE

By attaching a mercury manometer to the femoral artery, arterial blood-pressure records were made in the usual way at half-hour intervals. The general course of the blood pressure in a typical case of phosgene poisoning

^a The data in this chapter are based, in the main, on the experimental observations made by the detachment of the Medical Division of the Chemical Warfare Service on duty at the University of Wisconsin laboratory, account of which was published by Maj. W. J. Meek, C. W. S., and Lieut. Col. J. A. E. Eyster, M. C.: Experiments on the Pathological Physiology of Acute Phosgene Poisoning. *American Journal of Physiology*, Baltimore, Md., 1920, li, No. 2, 303.

may be seen at a glance by referring to Chart XIX. This composite curve, in common with those that are to follow, was made by dividing each of the experiments in the series into 10 equal periods. The animals lived an average of 16 hours after gassing. Each of the 10 intervals, therefore, represents on the average a little over one hour and a half. The data for the same period in all the experiments were averaged and the results plotted as a composite curve.

A few animals showed a slight fall of blood pressure after being taken from the gassing chamber. In most cases this was insignificant, and it did not lower the composite curve during the first period. As a rule the blood pressure gradually rose during the first half of the experiment, increasing some 10 per cent above the normal. Beginning with the sixth period, it began to fall slowly,

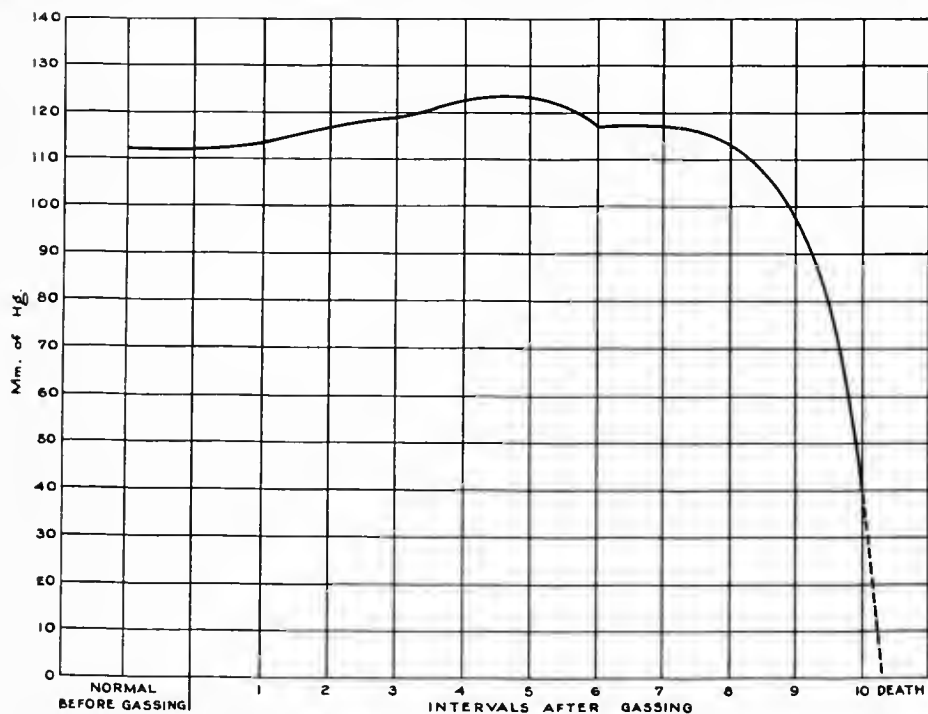


CHART XIX.—Composite curve, from ten experiments, of the changes in arterial blood pressure after acute phosgene gassing

reaching normal at the beginning of the eighth interval. Once having passed the normal the decline became extremely rapid and continued without intermission until the death of the animal. This break in blood pressure, which occurred at the eighth period, was an extremely striking event in all the animals studied. It made possible a very accurate prediction as to how much longer the animal would survive. Until its significance was fully appreciated, many of the animals died before final observations could be made.

Chart XX is a reproduction of the actual records from a typical experiment. The points just mentioned may be noted. The first record, at 11.10 a. m., was taken shortly after the gassing. The pressure then rose gradually for more than six hours. At 12.10 a. m., 13 hours after gassing, the pressure was still normal, though falling. One hour and twenty minutes later the animal was dead.

One need not attempt to interpret the arterial blood-pressure curve of acute phosgene poisoning until all the other data have been presented. Its resemblance to an asphyxial vasoconstriction, however, is obvious. That the rise may have been due to vasoconstriction and the fall in part to paralysis of the vasomotor center is suggested by the large vasomotor waves which so often occurred late in the blood-pressure tracings. (See Chart XX, the record at 12.45 a. m.)

VENOUS BLOOD PRESSURE

In the preceding series of 10 experiments venous pressure observations were made simultaneously with the arterial. These were secured by inserting a sound into the femoral vein. The sound was connected to a manometer and a reservoir of Ringer's solution. The pressure in the system was raised above what the reading was likely to be. On removing a clip the blood pressure was balanced against that of the fluid in the manometer. The reading could be made before there was any tendency to clot, and the fluid added to the blood stream at each observation was negligible.

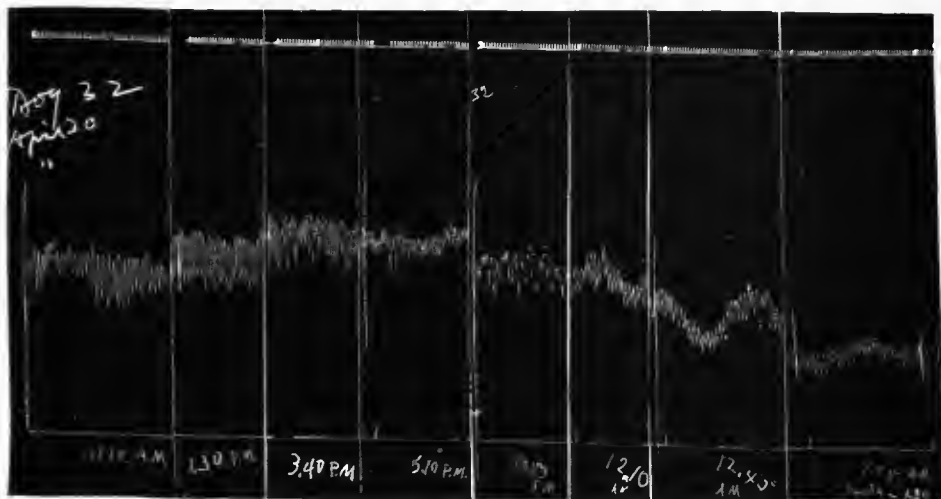


CHART XX.—Arterial blood pressure record from a case of acute phosgene poisoning

Venous pressure was found to be rather variable, conforming, on the whole, however, to what one might expect from the arterial. During the long period of increased arterial pressure, venous pressure was either normal or slightly below. In the terminal stages, however, it often rose markedly. In 2 of the 10 experiments there was a noticeable increase in venous pressure immediately after gassing. These were very severe cases, death occurring within nine hours. It would seem probable that in these animals the initial injury to the lungs was so great that the pulmonary circulation was obstructed and venous pressure therefore forced to rise.

PULSE RATE

Shortly after gassing the pulse rate fell in practically all cases. This occurred in animals morphined before gassing, as well as in those that received none of the drug. It was therefore an expression of the action of the poison itself. The decrease in rate brought the pulse from an average of 95 to 70 beats per

minute. By the time the experiment was half over the heart rate had returned to normal, and following this it was very markedly accelerated. Chart XXI presents a composite curve from 14 experiments in which the pulse rate was carefully followed. The final determination of the curve is the average of the highest rates obtained in the tenth period. As death became imminent, the heart rate became irregular and the rate then, of course, decreased. Electrocardiograms taken at this time showed various kinds of blocks, dropped beats and extra systoles, features which characterize most records taken during death by asphyxiation.

The pulse rate offered an excellent means of following the condition of the animal. Two of the dogs in one series recovered. The pulse curves from these

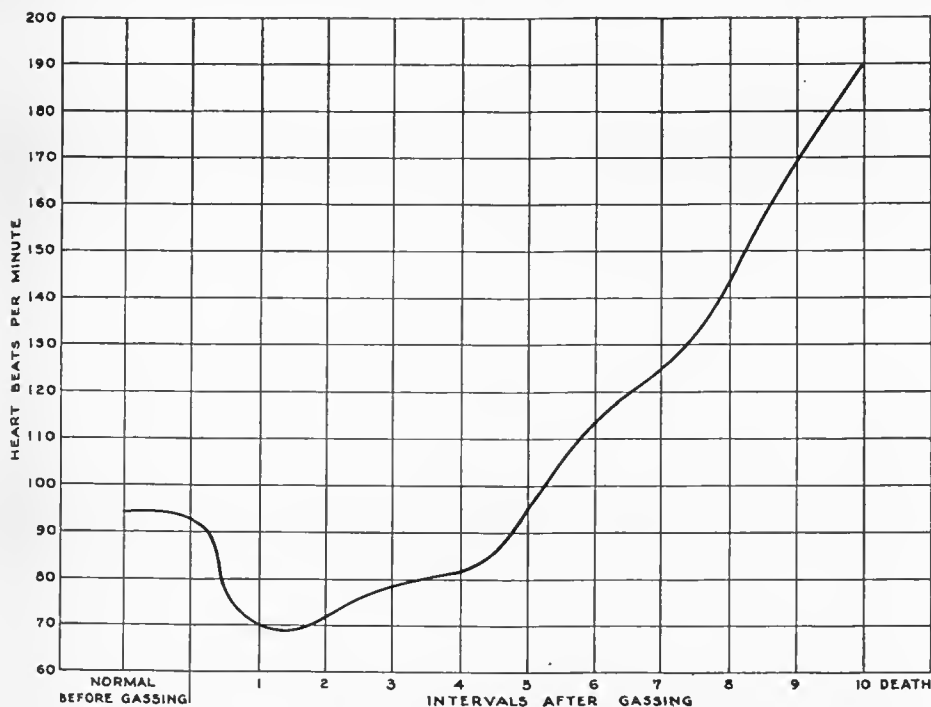


CHART XXI.—Composite curve from fourteen experiments, of the changes in the heart rate after acute phosgene gassing

animals were of special interest. There was the initial fall and the subsequent rise, but the latter never exceeded 120 beats per minute. A large number of observations have confirmed the opinion that a fatal outcome is to be expected if the heart rate continues to rise above 125 or 130 beats.

HEMOGLOBIN DETERMINATIONS

It was soon realized that there were very significant changes in the hemoglobin content of the blood in dogs suffering from phosgene poisoning. At death the blood was viscous, even tarry in consistency, and the hemoglobin readings showed an almost unbelievable concentration. Underhill¹ first pointed out that this stage of concentration was preceded by an initial one in which the hemoglobin content of the blood was decreased.

The characteristic hemoglobin changes during the course of the poisoning may be seen in Chart XXII. In an average experiment the hemoglobin readings were below normal during the first four periods of the experiment. This constitutes Underhill's first stage of phosgene poisoning. Concentration then began, and in the period preceding death the hemoglobin readings average over 150 per cent. The periods of concentration make up Underhill's second stage.

The maximum decrease in hemoglobin occurred anywhere during the first four periods; in other words, during the first five or six hours of the experiment. Since the maximum decrease did not occur in the same period for all the experiments, the composite curve does not show the lowest limit reached in hemoglobin concentration. In the 16 cases reported, it actually averaged

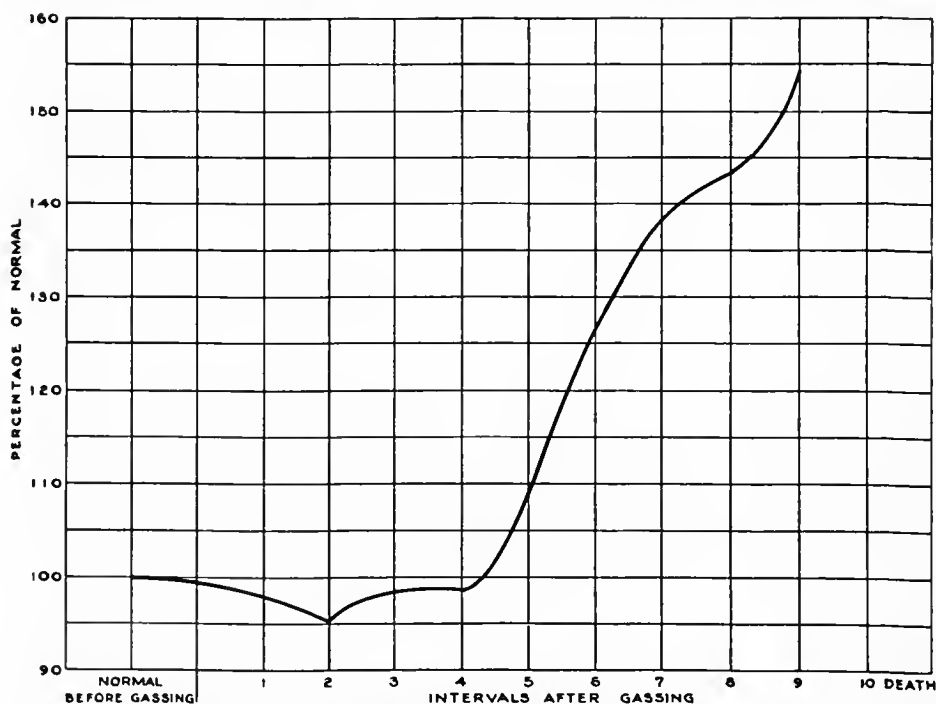


CHART XXII.—Composite curve from sixteen experiments, of the changes in hemoglobin concentration after acute phosgene gasping

11 per cent; that is, a hemoglobin reading of 89. The lowest reading noted was 85, although in a treatment series not here reported there were readings as low as 80 and one of 78. The maximum decrease lasted a very brief time and often there was difficulty in making desired observations at exactly the proper moment.

The degree of subsequent hemoglobin concentration always bore a definite relation to the severity of the poisoning and made possible a rather accurate prognosis. One hundred and twenty-five per cent may be said to represent a critical point. Any animal exceeding this figure was pretty sure to die in the course of the next five or six hours. If an animal was not gassed enough to reach this concentration, or if by any means a 125 per cent concentration could be prevented, there was an excellent chance for recovery.

Hemoglobin readings are usually interpreted in terms of the fluid content of the blood, or blood volume. If plasma or water has left the blood stream there is of course a concentration of hemoglobin, and if fluid has entered the blood stream from the tissues or elsewhere there is naturally a lowered hemoglobin content. While this is the general rule, there may be exceptions. Hemolysis or stagnation of red blood cells at any point might very greatly modify hemoglobin determinations and yet the blood volume would be entirely unchanged.

The natural interpretation of the hemoglobin curve for phosgene poisoning would be that in stage 1 there is an increase of blood volume and in stage 2 a marked decrease. That there is a real decrease in stage 2 is borne out by the fact that the lungs are now full of fluid which must, of course, have come from the blood. There is, however, no equally obvious explanation for an increase of blood volume in stage 1. Underhill ¹ also found in this stage a decrease in the blood chlorides, but the excess at the time in the urine and fluid of the lungs might account for this decrease.

BLOOD-VOLUME DETERMINATIONS

The blood volume was determined directly in eight animals during stage 1 and in three animals during stage 2. The technique used was the acacia method ² which has been developed in the laboratory of the University of Wisconsin. In Table 26 may be seen the results.

TABLE 26.—*Blood volume in phosgene poisoning*

STAGE 1		
Weight of animals	Hb. at time of determination	Blood volume in per cent of body weight
<i>Kilo-grams</i>	<i>Per cent</i>	
9.80	88.4	8.7
9.58	90.9	9.6
9.14	91.0	11.1
9.82	94.4	10.8
8.48	96.0	8.7
8.42	92.0	9.5
7.22	83.5	11.2
5.70	84.5	9.9
Average		9.9
STAGE 2		
14.00	-----	6.5
13.8	-----	8.1
13.5	-----	7.5
Average		7.3

The data presented give no evidence of a blood volume increase in stage 1. In a large series of normal dogs the volume was frequently 10 and 11 per cent of body weight, with an average of 9.7 per cent. The eight animals here investigated averaged, then, within 2 per cent of normal. Furthermore, of the three animals having the greatest hemoglobin dilutions, only one had a volume above the average.

In stage 2 only three determinations were made; unfortunately no hemoglobin readings were made simultaneously. Red blood-cell counts, which always paralleled the hemoglobin readings, indicated, however, that the latter were in the neighborhood of 135 per cent. Since the technique required the removal of 20 c. c. of blood, the determinations were made some time before the anticipated death of the animal. The figures, particularly the first and third, show that these animals had a marked decrease in blood volume. Even 8.1 per cent body weight is a lower blood volume than we have ever found in a normal dog.

Stage 1 of phosgene poisoning, on the grounds of blood-volume data, is believed to represent an actual decrease in the total hemoglobin content of the blood, a point which will be discussed later under histological examination

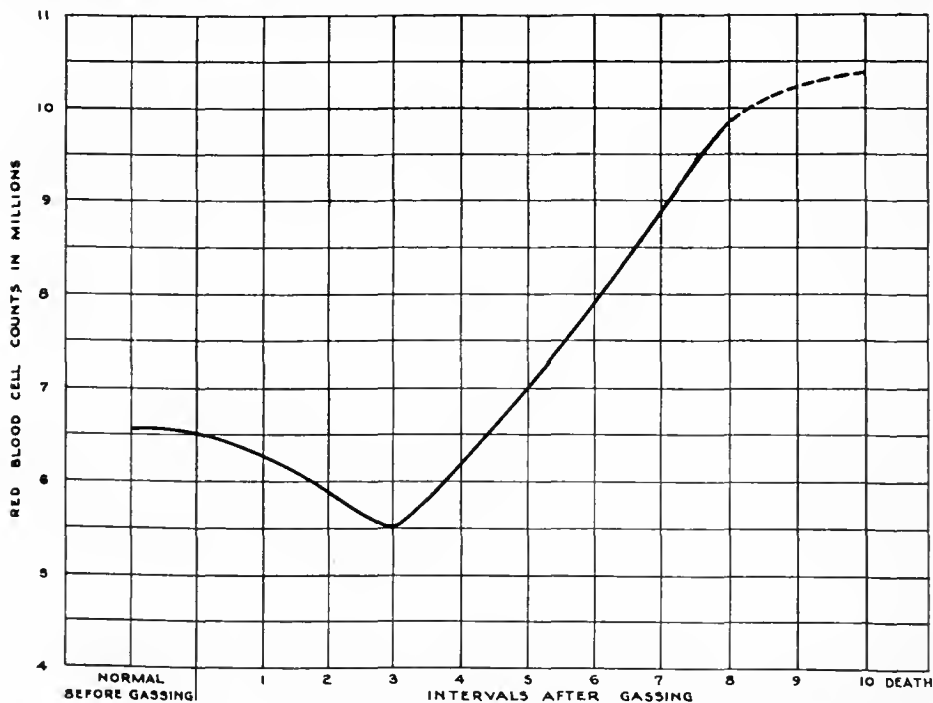


CHART XXIII.—Composite curve, from nine experiments, of the changes in the red blood cell counts after acute phosgene gassing

of the lungs. In stage 2 there can be no doubt that the blood volume is actually greatly decreased.

RED BLOOD-CELL COUNT

Little need be said concerning the red blood-cell counts other than that they uniformly paralleled the hemoglobin determinations. A composite curve from nine experiments may be seen in Chart XXIII. As in the hemoglobin curve, stages 1 and 2 are evident, and they occupy the same relative positions.

HISTOLOGICAL EXAMINATION OF THE LUNGS

Careful histological examinations of lung tissue were made in a series of poisoned dogs.^b Special methods for fixing and staining pulmonary tissues

^b These examinations were made by Dr. W. S. Müller, of the Department of Anatomy, University of Wisconsin.

were used, rather than the routine technique of general pathology. These examinations showed that the injury from phosgene was almost exclusively in the lower respiratory passages. There was constriction or spasm of the small bronchioles, with the accompanying atelectasis and emphysema, and edema of the connective tissue. The alveoli were irregular, their membranes were injured, and in many cases they contained exudate. Very important from the point of view of these studies was the extensive clogging of the capillaries with red blood cells. Even small veins were solidly plugged. In many cases these masses in the veins had shrunk slightly and the surrounding clear areas were filled with serum. That these changes in the lungs were not post-mortem is substantiated by the fact that they were characteristic of all the early stages of poisoning and that they were found after every attempt to avoid post-mortem clot.

Furthermore, if phosgene in a dilution as great as 1 to 20,000—that is, 0.222 milligrams per liter—was bubbled through a 2 per cent suspension of defibrinated dog's blood, there was in 20 minutes a marked agglomeration of the red corpuscles. This is direct evidence that the gas has the power of doing just what the histological picture shows.

In slightly later stages than the one figured, there was evidence that compensatory paths were being opened up for the blood stream. Capillaries which were not plugged were widened and others had been dilated sufficiently to allow a flow of fluid around the obstructions.

The importance of these histological findings on the physiological conception of phosgene poisoning is at once apparent. The plugged capillaries and veins at first must have greatly increased pulmonary resistance and the work of the right heart. Later there was relief by the development of compensatory passages. Just how the heart reacted to this will be seen in the following section. Furthermore the injuries to the alveolar walls must have decreased the exchange of gases between the blood and the alveolar air.

HEART SIZE

In a large series of experiments, stereoscopic examinations and X-ray photographs of the thorax were made at frequent intervals. At first the outline of the heart was sketched in with a grease pencil on the glass cover of the fluoroscope. Later stereoscopic plates were made and these, of course, proved much more reliable than the former method. To be sure that the animal was in the same position for each photograph, a lead cross was sewed to the chest and the center of this brought under a plumb bob at each exposure. Exposures were always made during the same phase of respiration, preferably inspiration, and the flashes were long enough to insure that it was the diastolic size of the heart which was secured.

These observations showed two interesting and important changes in heart size during acute phosgene poisoning. There was, first, immediately after removal from the gas chamber, an increase in the size of the heart which varied considerably in degree, but which was always associated with a relative enlargement of the right auricle and ventricle. This condition persisted for several hours and might even increase for an hour or more.

By the beginning of the fourth period, assuming that the experiment had been divided into 10 equal intervals, a second change appeared which was a gradual reduction in heart size. This seemed to appear first in the left ventricle, but soon the whole heart became distinctly smaller. It assumed a pendular shape which was apparently identical with that following severe hemorrhage, as determined in control experiments. This decrease in size continued during the development of the extensive pulmonary edema. During the period of asphyxial death the heart began to enlarge, particularly the right side, and after the death plates invariably showed a dilated heart with relative increase of the right side.

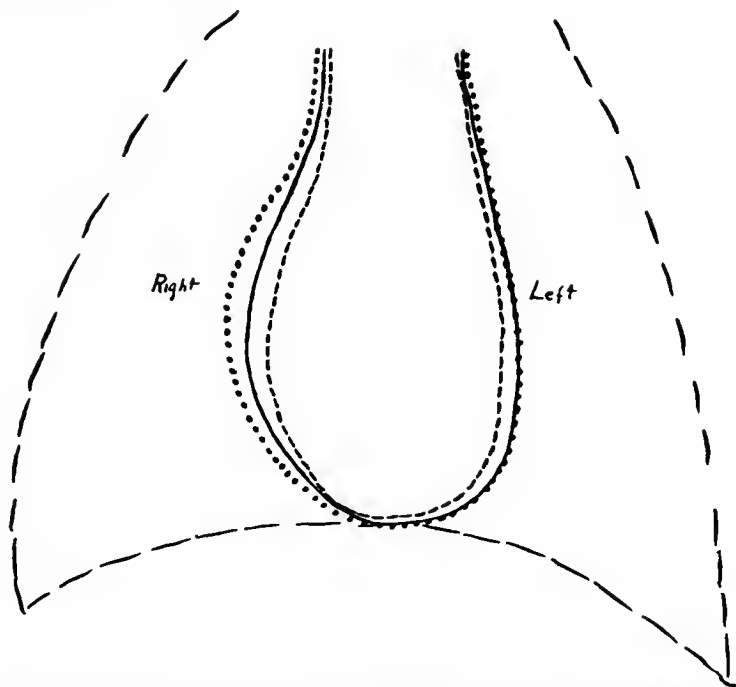


FIG. 45.—Superimposed outlines of three X-ray photographs taken at intervals during phosgene poisoning to show changes in shape of the heart. The solid line indicates the normal. The dotted line shows the right-sided dilatation 39 minutes after gassing. The broken line is from a photograph taken 11 hours and 53 minutes after exposure to the gas. The heart had then become pendular in shape and much reduced in size.

Figure 45 illustrates strikingly the stages of increase and decrease in heart size. The area of the normal heart shadow as determined by the planimeter was 51.2 sq. cm. Thirty-nine minutes after gassing, the area had increased to 55.4 sq. cm. Eleven hours and fifty-three minutes after exposure the heart had decreased to 44.5 sq. cm. This was at a time when the pulmonary edema had become very marked.

CHANGES IN THE LUNGS

The condition of the lungs was determined in a large number of animals by means of physical, fluoroscopic, and stereoscopic X-ray examinations. Immediately after removal from the gas chamber there was noted a diffuse clouding of the lungs, usually most marked in the middle and upper lobes, but

sometimes involving the lower lobes also. This was accompanied by an increase in density and number of the streaky shadows cast by the larger bronchi and vessels at the roots of the lungs. For a few hours the cloudy appearance of the lungs generally increased slowly without being associated, however, with any constant physical signs. Occasionally transitory fine, dry, crackling râles were heard during expiration, and occasionally there was a slight roughening of the normal respiratory sounds.

After these few hours the lungs often appeared somewhat clearer. This improvement, however, was transient and gave way during the latter third of the experiment to a streaky, mottled appearance, at first marked near the roots of the lungs but later involving the whole of both lungs. Often the heart outline was in part lost or obscured. It was at this time that numerous râles of all varieties made their appearance, medium moist predominating. These were heard in both inspiration and expiration. In brief, the clinical signs were now those of extensive pulmonary edema and passive congestion.

In the later stages there was frequently an impairment of the percussion notes, most evident in the pendant portions, and an extension of deep cardiac dullness, especially on the right side. X-ray plates showed, however, that this was not due to cardiac enlargement but probably to better transmission of heart dullness by the edematous lung.

There were thus three more or less distinct changes to be made out by means of the X ray in the lungs of animals fatally poisoned with phosgene. First a diffuse cloudiness due probably to the initial epithelial injury and to the agglomeration of the corpuscles in the capillaries. Second, an improvement, a decrease in the cloudiness, accounted for by a reopening of many of the capillary passages. Third, a marked increase in the density and extent of all shadows cast by bronchi and blood vessels and an extension of the mottled appearance to all parts of the lungs. It is worthy of mention that it was only during the third stage that the classical clinical signs of pulmonary edema developed. The X ray proved a much more delicate method of following lung lesions than the older methods of percussion and auscultation.

RESPIRATORY RATE AND PULMONARY AERATION

One of the earliest results of phosgene gassing was an increase in the respiratory rate. By the end of the fourth period, that is stage 1, the rate had usually increased from an average of 30 to 45 per minute. This increase continued through stage 2 until the death period itself, when the respirations, of course, became irregular and gradually less rapid.

Respiratory rate, particularly in the dog where there may be much panting, gives a poor idea of the amount of air actually passing in and out of the lungs. To secure such data a series of five experiments was run, in which the dogs were placed in an air-tight rigid chamber that inclosed the entire animal except the head. An inflated rubber collar secured an air-tight fit around the neck. The box was connected by tubing to a piston recorder which not only made a record of the respiratory rate but on calibration gave an accurate measure of the air passing in and out of the lungs.

The data thus secured, as shown in Table 27, indicate in all cases a final marked increase in pulmonary aeration. In all cases the amount of air respired was at least doubled in the latter periods of the poisoning. Even after the

break in arterial pressure when respirations often slowed down, the increase in aeration was maintained. In three cases the amount respired immediately after gassing was definitely lower than normal.

TABLE 27.—*Pulmonary aeration during phosgene poisoning*

[Aeration in cubic centimeters per minute]

Experiment No.	Normal	Immediately after gassing	About 1 hour before death
34.....	1,360	420	3,000
35.....	1,265	850	2,501
36.....	950	1,540	2,080
37.....	1,175	1,650	2,660
38.....	1,370	1,060	3,080

TEMPERATURE

The only constant change in temperature was a gradual fall as blood concentration increased and death became imminent. This amounted to as much as 2° in many cases. Very frequently there was a slight initial rise in temperature during stage 1.

ALKALINE RESERVE

Our studies on alkaline reserve were very incomplete. Determinations taken at irregular intervals in 11 experiments seem, however, to justify the statement that there was no change of particular significance until the latter periods of the experiment. At about the time blood pressure fell so markedly there was a decided decrease in the alkaline reserve. The tissues at that time were undoubtedly suffering from oxygen want and the decrease in carbonate was due to the formation of fixed acids.

DISCUSSION

The various pathological physiology studies just reported are of interest chiefly in giving a conception of phosgene poisoning as a whole. In fatal cases, and these studies were made on such, two rather well-marked stages were apparent. The first of these was characterized by the nervous reflexes due to the irritation of the gas in the respiratory passages and by the direct chemical action of the gas or its decomposition products on the blood. The second stage was characterized by well-developed pulmonary edema and its natural consequences. The whole subject, indeed, might well be termed a study of pulmonary edema induced by phosgene.

The first effect of the gas was to injure the linings of the deep respiratory passages. Spasm of bronchiole musculature was evidence of the stimulation produced by the fumes. As a result of this there was a reflex cardiac inhibition, very characteristic of many stimulations of the respiratory surfaces. The composite curve of heart rates shows a decrease during the first half of the poisoning. Another reflex from the same cause was a vasomotor one which brought about peripheral constriction, with a rise in blood pressure. The X ray gave evidence of pulmonary injury at this time although physical signs were usually entirely absent. More important than these nervous phenomena, however, is the direct action of the gas on the blood in the pulmonary capillaries. Here the red corpuscles were agglomerated into masses which largely

filled and blocked the capillary passages. Bubbling gas through blood showed that it might have just this effect. The results of this plugging of the capillaries were twofold. In the first place pulmonary resistance was increased and a load thrown upon the right heart. Evidence of this was seen in the right cardiac dilatation found in the X-ray plates. A second result was the removal of red cells from the circulation, which resulted in a decreased hemoglobin content of the blood. This first stage of phosgene poisoning, as shown by Underhill,¹ is most easily determined by following the hemoglobin, and it may be spoken of as the stage of decreased hemoglobin concentration.

Underhill explained the decreased hemoglobin concentration on the basis of blood dilution by body fluids. Just how or why blood volume should be increased at this time is not clear. That this interpretation is probably not sufficient is shown by direct determinations which indicate no increase in blood volume, and by the histological examination which show the red cells agglomerated in the capillaries.

Long before the end of the first stage pulmonary edema was under way. The direct cause of this was undoubtedly the increased permeability of alveolar and capillary walls, due to direct injury from the gaseous fumes. The increased pulmonary blood pressure resulting from the capillary plugging greatly favored the condition.

The second stage of acute phosgene poisoning was characterized by rapid development of the pulmonary edema with all its physical signs. This resulted in a decreased blood volume and increased hemoglobin concentration and a smaller diastolic size of the heart. The essential thing was the greatly reduced blood volume, which is almost entirely accounted for by the increased fluid in the lungs.

Death under such conditions obviously may be accounted for in either one of two ways. The edematous condition of the lungs may interfere with the gaseous exchanges to such an extent that the animal asphyxiates, or the blood volume may be so reduced that even though the hemoglobin is oxygenated there is not enough fluid to secure its proper distribution to and circulation in the tissues. So far as the tissues themselves were concerned the result was the same. They died of oxygen starvation. Death was probably due to a combination of the two causes. This belief is based on a series of experiments in which gassed animals were immediately placed in chambers containing 40 to 60 per cent oxygen. The carbon dioxide content was of course kept within physiological limits and oxygen supplied automatically so as to keep the amount constant. The majority of these animals lived from 48 to 72 hours instead of the average 16 and seemed to be recovering. On being released the usual occurrence was for each dog to walk across the room and fall into an asphyxial convulsion, which quickly terminated in death. Several of the animals were hurried back into the oxygen chamber and resuscitated. These animals were edematous with reduced blood volumes, but in an atmosphere of 40 per cent oxygen life was preserved, one is tempted to believe, because of complete hemoglobin saturation and physical absorption of oxygen. That decreased blood volume is a cardinal part of the syndrome, and possibly by far the most important part, need not be questioned.

SUMMARY

1. A study of the pathological physiology of acute phosgene poisoning shows a well-marked succession of events which finally results in typical pulmonary edema. The microscope and the X ray both show an early injury to the linings of the deep respiratory passages. Irritation from this results in a certain amount of reflex cardiac inhibition and vasoconstriction. Coincident with these changes there is a direct action of the gas on the red blood cells, which causes them to agglomerate and obstruct the pulmonary capillaries. The removal of red blood cells from the active circulation in this way results in a decreased hemoglobin percentage. The plugging of the capillaries throws a strain on the right heart and a right-sided cardiac dilatation is apparent. These are the chief characteristics of stage 1.

2. Even during stage 1 the injury to the alveolar membranes and the increased pressure have initiated the transfusion of fluid from the blood into the tissue spaces and later into the air passages of the lungs. The rapid development of the edema is the chief characteristic of stage 2. It results in hemoglobin concentration, reduction in blood volume and decrease in heart size, all three of which proceed to extreme degrees. Death ultimately results from decreased oxygenation of the pulmonary blood and from oxygen starvation of the tissues due to decreased blood volume, the latter being probably the more important.

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- (2) Meek, W. J., Gasser, H. S., and Erlanger, J.: *Studies in Secondary Traumatic Shock*. *American Journal of Physiology*, Baltimore, Md., October, 1919, 1, No. 1, 31.

CHAPTER XII

PHYSIOLOGICAL ACTION OF DICHLORETHYLSULPHIDE (MUSTARD GAS)^a

When an animal was exposed to the vapors of dichlorethylsulphide in high concentration it subsequently showed a complex of symptoms which may be divided into two classes: (1) The systemic effects due to the absorption of the substance into the blood stream and its distribution to the various tissues of the body. These effects were not generally recognized. (2) The local effects on the eyes, skin, and respiratory tract. These were well recognized, and consisted mainly of conjunctivitis and superficial necrosis of the cornea; hyperemia, edema, and later, necrosis of the skin, leading to a skin lesion of great chronicity; and congestion and necrosis of the epithelial lining of the trachea and bronchi.

The most striking observation regarding the symptoms of dichlorethylsulphide poisoning was the latent period, which elapsed after exposure before any serious objective or subjective effects were noted. The development of the effects was then quite slow, unless very high superlethal doses had been inhaled.

SYSTEMIC EFFECTS

The symptoms observed in dogs when subjected to the vapors of dichlorethylsulphide which might suggest absorption into the blood stream through lungs and skin, and a systemic effect, were vomiting, diarrhea, hyperexcitability and convulsions, and effects upon the heart. Moreover, the condition of the lungs and trachea found at autopsy of some animals dying from the inhalation of the gas was not sufficient to account for death.

ABSORPTION THROUGH THE LUNGS

INJECTIONS

In order to become familiar with the effects of the absorption of dichlorethylsulphide into the system, dogs were injected with the substance. The simplest method of introducing the substance was by subcutaneous or intramuscular injection of olive oil solutions. The effects observed on an unanesthetized animal from the injection of a lethal dose in olive oil were, after a latent period, salivation, hyperexcitability, and convulsions, diarrhea, slow and irregular heart, which became rapid before death, muscular weakness, and finally coma and death.

^a The data in this chapter are based on the researches of the pharmacological research section, Medical Division, Chemical Warfare Service, conducted in the American University Experiment Station Laboratories, Washington, D. C., and published as follows: (1) Lynch, Vernon, Smith, H. W., and Marshall, E. K., jr.: On Dichlorethylsulphide (Mustard Gas). I. The Systemic Effects and Mechanism of Action, *Journal of Pharmacology and Experimental Therapeutics*, Baltimore, Md., 1918, xii, No. 5, 265; (2) Marshall, E. K., jr., Lynch, Vernon, and Smith, Homer W.: II. Variations in Susceptibility of the Skin to Dichlorethylsulphide. *Ibid*, 291; (3) Smith, Homer W., Clowes, George H. A., and Marshall, E. K., Jr.: IV. The Mechanism of Absorption by the Skin. *Ibid*, 1919, xiii, No. 1, 1.

The following protocols illustrate the effects of subcutaneous and intramuscular injections in olive oil solution:

EXPERIMENT 1.—Dog V7, male; weight, 12.5 kilos.

March 12.

- 10.15. Pulse 136, respiration 18.
- 10.28. Subcutaneous injection of 500 mgm. dichlorethylsulphide in 5 grams olive oil.
- 10.45. Behavior normal. Licks point of injection.
- 11.00. Somewhat restless.
- 12.00. Salivation, vomiting, diarrhea.
- 1.15. Pulse 66, respiration 32.
- 1.30. Muscular spasms, especially in hind legs. Convulsions. Animal staggers. Finally unable to walk.
- 1.40. Intraperitoneal injection of 3 grams chloretone in olive oil.
- 2.10. Pulse 66 (very strong), respiration 56. Still excitable.
- 2.45. Pulse 64, respiration 36.
- 4.15. Pulse 126, respiration 26. Given another injection of 500 mgm. sulphide.
- 5.00. Animal conscious, but unable to stand.

March 13. Found dead.

Autopsy.—Lungs and trachea appear normal; stomach contains bile and bloody fluid; intestines congested with few areas of hemorrhage and contain bloody fluid.

EXPERIMENT 2.—Dog V10, female; weight, 10 kilos.

- 9.50. Pulse 88, respiration 18.
- 9.55. Subcutaneous injection of 1,000 mgm. of dichlorethylsulphide in 10 c. c. of olive oil, 5 c. c. on each side.
- 10.00. Pulse 90, respirations 20. Animal quiet.
- 10.15. Restless.
- 10.30. Pulse 118, respiration 44.
- 10.50. Pulse 112, respiration very rapid, slight salivation.
- 11.15. Salivation, rapid respiration, diarrhea.
- 12.00. Pulse 44, respiration 102. Animal has previously had very good control of muscles. Movements are now stiff, convulsive, and uncontrolled. Tries to struggle to feet, but topples over and paws ground convulsively.
- 1.00. Pulse 36 (very strong, but irregular), respiration 112.
- 1.45. Pulse 36, respiration 64. Very weak, unable to rise. Has vomited.
- 2.40. Pulse 54, respiration 82. Vomiting. Now perfectly quiet.
- 3.00. Pulse 72, respiration 66.
- 3.20. Pulse 108 (very weak), respiration 54.
- 3.30. Dies.

Autopsy.—Trachea and lungs appear slightly congested; stomach filled with bloody fluid; intestines congested and hemorrhagic; other organs appear normal.

EXPERIMENT 3.—Dog DM203; weight, 17 kilos.

September 23.

- 10.30. Pulse 88, respiration 18.
- 10.35. Intramuscular injection of 240 mgm. (14 mgm. per kilo) of dichlorethylsulphide in 12 c. c. of olive oil.
- 11.00. Behavior normal. Pulse 114, respiration 30.
- 11.30. No toxic symptoms as yet. Pulse 100, respiration 20.
- 12.00. Pulse 102, respiration panting; is becoming hyperexcitable; appears irritable and trembles slightly, but walks without ataxia.
- 12.45. Pulse 120, respiration 28. Walks uncertainly; salivated; pupils normal. Injected leg affected, seems sore, and dog refuses to use it in standing or walking.
- 1.10. Pulse 120, respiration 30. Injected leg no longer seems sore, but is wholly useless.

- 1.45. Pulse 130, respiration 36. Though seemingly conscious, movements are decidedly convulsive. No diarrhea, great salivation or hyperexcitability. Pupils are now greatly dilated.
- 2.00. Pulse 114, respiration 29. Dog exhibits twitching and slow convulsive movements. Knee reflex in injected leg about normal; the leg is inactive during convulsive movements. Very irritable and snappy at times; then again is very affectionate. After drinking heavily, pulse runs up to 150, but is very irregular.
- 2.45. Pulse 144, respiration 60. Shows slight salivation.
- 4.20. Pulse 174, respiration 66. Still shows slight convulsive tendencies.

September 24.

- 9.00. Pulse 192, respiration 48. Dog is conscious, but trembles greatly. No salivation or evidence of diarrhea. Pulse varies greatly during day.

September 25.

- 1.00 No marked change in condition. Pulse running 150 to 180 throughout day, respiration 24 to 35.

September 26.

- 10.20. Pulse 156, respiration 32.

- 4.00. Dog found dead 77 hours after injection.

Autopsy.—Conjunctivitis; slight cutaneous edema at site of injection. Tracheal blood vessels congested; lungs apparently normal, with slight post-mortem changes. No hemorrhages in adrenal cortex. Liver, kidneys, and spleen normal; mucous membranes of gut hemorrhagic and bloody, chiefly in upper tract; stomach normal.

EXPERIMENT 5.—Dog DM202; weight, 11 kilos.

September 23.

- 10.30. Pulse 102, respiration 66.

- 10.40. Intramuscular injection of 220 mgm. (20 mgm. per kilo) of dichlorethyl-sulphide in 5.5 c. c. of olive oil.

- 11.00. Dog appears normal, except for panting. Pulse 138.

- 11.30. Pulse 100, respiration still panting.

- 12.00. Pulse 78, respiration 60. Marked salivation; appears spasmodically ataxic, with severe tremors; distinctly hyperexcitable.

- 12.45. Pulse 78, respiration very irregular. Salivation, but no diarrhea or vomiting. Exhibits severe convulsions. Pupils dilated. Injected leg stiff and does not enter into convulsive movements, which are of a clonic nature; between convulsive spasms, dog attempts to rise, but both rear legs are inactive.

- 1.10. Pulse 75, respiration 70. Passes small quantity of semiliquid stool without blood stain.

- 1.45. Pulse 68, respiration 36. No continued diarrhea.

- 2.00. Pulse 66, respiration 30. Heart sounds hammer-like, but very irregular in periodicity and intensity.

- 2.15. Pulse 90, respiration 28. Dog attempts to drink with great effort, but can not rise or put nose in water. Continues to lap air. Portrays marked muscular weakness and incoordination.

- 2.30. Pulse 68, respiration 39. Eyelids twitching. Reflexes abnormally active. Heart irregular, missing every third beat.

- 2.45. Pulse 150, respiration 40.

- 3.00. Pulse 150, respiration 48. Heart sounds becoming very faint, with increased rate.

- 4.00. Pulse 162, respiration 38. Great muscular weakness. Almost unconscious. Seems to be passing into coma.

- 4.20. Pulse 192, respiration 48. Dog lies in coma.

September 24.

- 12.00. Found dead after 13 hours.

Autopsy.—Trachea slightly congested. Lungs show small circumscribed points of hemorrhage throughout; considerable post-mortem congestion; adrenals show slight cortical inflammation. Kidneys normal, except for slight post-mortem congestion. External gut has too much post-mortem change to describe extent of external hemorrhage. Stomach is slightly congested. Very marked hemorrhage in the lumen of jejunum and duodenum; entire gut blood stained throughout. Injected leg showed great subcutaneous edema but no muscular changes beyond a slightly brighter color than in normal leg.

The intravenous injection was much more instructive but somewhat more difficult. The slight solubility of the substance in water (about 0.07 per cent at 10° C.), and the rapidity with which an aqueous solution hydrolyzes were the main difficulties. This could not be overcome by the injection of an alcohol or acetone solution, for as soon as these solutions came in contact with water the sulphide was precipitated out as fairly large oil droplets. These difficulties were overcome by the injection of large amounts of a freshly prepared, cold, saturated aqueous solution.

The method of preparing the aqueous solution for intravenous injection was as follows: Five hundred cubic centimeters of 0.8 per cent saline was cooled to 8 to 10° C. This was placed in a flask, about 1 c. c. of pure dichloroethylsulphide was added, the flask tightly stoppered, and shaken for about one minute. The contents of the flask were transferred to a separatory funnel and the oil allowed to settle. An oil film was present on the surface as well as globules at the bottom. About 400 c. c. of solution was removed from between the oil and film, care being taken to obtain a solution free from oil films or droplets. This was placed in a bath at 8 to 10° C. and used as soon as possible. The solution prepared in this way contained about 0.7 mgm. per cubic centimeter.

The hydrolysis of the aqueous solution is a monomolecular reaction. At 10° C. only about 15 per cent of the disulphide is hydrolyzed in 10 minutes, while at 37.5° C. over 97 per cent is decomposed in the same time.

The symptoms elicited from an intravenous injection were similar to those observed from the subcutaneous injection of olive-oil solutions. While the solution was being injected, and for some time after, the animal showed no effects whatever. A record of the blood pressure, pulse, and respiration failed to show an appreciable effect at this time.

Within 10 to 20 minutes after injection, however, an increased salivation was noticed. This soon developed into a very free flow of rather mucinous saliva. The next symptom observed was usually a diarrhea, which might be accompanied by vomiting. This diarrhea was present until the death of the animal, and a few hours after the injection the stools frequently contained blood. After injection the respiration became rapid, and if anesthesia had not been used the animal showed a distinct hyperexcitability. At this stage he might be frightened by a slight movement of the hand or unexpected touch, and the eye reflex might be obtained by touching almost any part of the face. The gait soon became unsteady, movements of the muscles were spasmodic but uncontrolled, and apparently accompanied by tetanic contractions of the antagonist. The knee-jerk might be elicited by a touch of the finger. The animal soon became unable to walk or even to stand, and the violent spasmodic movements increased to the stage of convulsions, with extension of the hind legs and arching of the neck and back. The pulse, which might have been somewhat slowed, soon became irregular. Palpation suggested that the heart was dropping a beat occasionally. The dropped beat became more and more frequent until finally the heart was beating at one-half its former rate. If the chest was opened it was clearly seen that the ventricles were beating once to every two beats of the auricles. Later the rhythm might even become 1 to 3. Stimulation of the vagi showed some apparent hyperexcitability. The blood pressure fell very slowly, and a few hours before death the heart resumed

its normal rate. At this stage, or before, it was found that the heart could not be slowed or in any way affected by strong stimulation of the vagi, although the respiration was easily inhibited. Section of the vagi had no effect upon the heart rate except a slight slowing. Apparently the vagus endings were paralyzed. The heart became feeble, there was a great dilatation in the splanchnic area, a high venous pressure, and the arterial blood pressure was falling slowly. The convulsions ceased, and the animal lay in a coma. Death came quietly in less than 24 hours after the injection and was probably due to the weakening of the heart and the great dilatation of the vessels in the splanchnic area. Autopsy revealed a more or less intense congestion of the intestinal mucosa which might extend from the pylorus to the anus, and was frequently accompanied by hemorrhage into the lumen of the intestine. The condition suggested the excretion of the dichlorethylsulphide into the intestine. These effects upon the heart, the alimentary tract, and the central nervous system were quite characteristic and unmistakable.

The following protocols are representative of the course of an intravenous injection. In all cases the cold, saturated aqueous solution, prepared as described above, was used. The solution was usually injected within 10 to 15 minutes after its preparation. When injected such a solution contained about 0.5 to 0.6 mgm. of undecomposed dichlorethylsulphide to each cubic centimeter.

EXPERIMENT 6.—Dog, V9, female; weight, 8.2 kilos.

11.40. Pulse 88, respiration 16.

11.50–12.00. Injection into jugular vein of 120 c. c. fresh aqueous solution (14 c. c. per kilo).

12.05. Shivering. Pulse 160, respiration 66.

12.20. Slight salivation, has vomited. Pulse 70, respiration 74.

12.45. Diarrhea, no blood. Pulse 52 and irregular, respiration 108.

1.20. Highly excitable, convulsions, readily thrown into spasms—comparatively quiet between.

1.45. Pulse 80, respiration 110.

2.15. Pulse 86, respiration 120.

2.45. Pulse 84, respiration 120.

3.45. Pulse 84, respiration 110. Struggling, profuse salivation, has had diarrhea for some time.

3.50. Killed with ether.

Autopsy.—Trachea appears normal. Lungs very small area of congestion in one lobe, a few emphysematous patches. Esophagus and stomach appear normal. Duodenum, congested areas beginning at pylorus. Small and large intestine show distinct congestion.

EXPERIMENT 7.—Dog V17, female; weight, 5.5 kilos.

March 29.

3.10. Pulse 120, respiration 12.

3.12–3.20. Intravenous injection of 120 c. c. of cold, aqueous solution (22 c. c. per kilo).

3.25. Pulse 150, respiration 42.

3.35. Pulse 120, respiration 198. Trembling, good control of movements.

3.45. Vomiting; diarrhea.

4.05. Gait very unsteady.

4.30. Vomiting; fluid stools.

4.50. Struggling, convulsions begin; salivation.

5.00. Still in convulsions.

March 30.

9.00. Found dead.

Autopsy.—Trachea slightly congested; lungs appear normal; heart, large, endocardial hemorrhages; stomach contains bloody fluid; duodenum very deep red, bloody contents; small and large intestine deeply congested.

EXPERIMENT 8.—Dog V36, male; weight, 9.5 kilos.

April 22.

- 10.45. Pulse 90, respiration 11.
- 11.02–11.05. Injection of 95 c. e. fresh, aqueous solution into jugular vein.
- 11.16. Slight salivation, vomiting.
- 11.25. More vomiting.
- 11.40. Hyperexcitability.
- 12.45. Convulsions.
- 1.00. Pulse 120, respiration 30, convulsions.

In the following experiments the dose given was too small to produce convulsions, but the other symptoms were observed.

EXPERIMENT 9.—Dog V20, male; weight, 11 kilos.

April 2.

- 12.18. Pulse 120, respiration 24.
- 12.18–12.23. Injection of 66 c. e. cold, fresh aqueous solution in jugular vein.
- 12.25. Pulse 116, respiration 21.
- 12.30. Perfectly normal.
- 1.05. Has vomited.
- 2.00. Pulse 120, respiration 20; normal movements.
- 3.00. Pulse 132, respiration 24; salivation; lying quietly, but leg muscle twitched a good deal.

April 3. Apparently normal; killed for autopsy.

Autopsy.—Lungs appear normal; duodenum congested and slightly hemorrhagic; small intestine contains bloody contents.

EXPERIMENT 10.—Dog V34, male; weight, 7.2 kilos.

- 9.45. Pulse 96, respiration 12.
- 10.05. Intravenous injection of 36 c. e. cold, fresh aqueous solution (5 c. e. per kilo).
- 10.08. Pulse 108, respiration 14.
- 10.55. Has vomited.
- 11.05. Slight unsteadiness of gait.
- 2.25. Pulse 132, respiration 32. Gait normal.

EXPERIMENT 11.—Dog V19, female; weight, 17.3 kilos.

April 1.

- 12.55. Pulse 138, respiration 18.
- 1–1.05. Injection intravenously 34 c. e. of cold, fresh aqueous solution.
- 3.00. Pulse 78, respiration 12, quiet.

April 2.

- 9.00. Depressed, very quiet, refuses food. Killed for autopsy.

Autopsy.—Lungs appear normal; duodenum congested, bloody mucous abundant; small intestine congested; large intestine normal.

The following protocol is illustrative of the symptoms of an animal injected very slowly. The symptoms were the same as when injection was made rapidly, but appeared to be somewhat more delayed and milder.

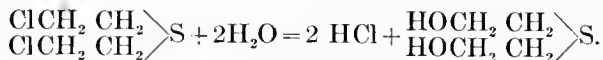
EXPERIMENT 12.—Dog V16, male; weight, 4.5 kilos.

- 1.30. Pulse 150, respiration 18.
- 1.55–2.55. Intravenous injection of 100 c. e. cold, fresh aqueous solution (22 c. e. per kilo).
- 2.54. Pulse 125, respiration 48, slight salivation.
- 3.00. Pulse 120, respiration 78, salivation, seems excitable, defecated, bad control of movements.
- 3.30. Pulse 120, respiration 55, bad control of movements, diarrhea.
- 3.45. Pulse 60, respiration 84, moves around fairly well.
- 4.00. Movements unsteady and spasmodic, convulsions begin.
- 4.05. Unable to stand.
- 5.00. Respiration 72, lying prone in convulsions.

March 30. Found dead.

Autopsy.—Trachea normal; lungs, one lobe appears congested; duodenum, deeply blood-stained contents; intestines congested with blood-stained contents; heart, few small subendocardial hemorrhages.

The injection of saturated aqueous solutions, which have been allowed to come to room temperature or which have been standing for any time, showed much diminished effects, or, if several hours old, were entirely without effects. This was tried by intravenous injection and also on the eye and skin. Such solutions were known to be partially or completely hydrolyzed into hydrochloric acid and dihydroxyethylsulphide.



EXPERIMENT 13.—Dog V11; weight, 4 kilos.

March 22.

3-3.15. Injection intravenously of 160 c. c. aqueous solution 24 hours old (40 c. c. per kilo).

4.00. No effects.

6.00. No effects.

March 23.

9.00. Dog perfectly normal. No vomiting or diarrhea during night.

EXPERIMENT 14.—Dog EM970; weight, 8 kilos.

2.40. Pulse 130, respiration 18.

2.50. Intravenous injection of 10 c. c. per kilo of a saturated aqueous solution of dichlorethyl-sulphide which had stood for three and one-half hours.

3.00. Pulse 160, respiration 18.

3.50. Pulse 160, respiration 22; dog seems normal.

4.15. Pulse 164, respiration 20. Animal appeared perfectly normal while under observation for two or three days.

EXPERIMENT 15.—The cold, fresh, aqueous solution was applied to the forearms of five men. After standing at room temperature for two hours it was again applied. Twenty-four hours later, four out of five of the men showed a distinct reaction from the fresh solution, none exhibited any effects from the solution two hours old.

EFFECTS OF INHALATION OF LARGE DOSES OF THE VAPOR

Some of the effects which have been observed from the injection occurred when a dog was poisoned by inhalation of the vapor. When a dog was poisoned by inhalation of a very large dose of the vapor, practically all the effects obtained by injection (salivation, vomiting, bloody diarrhea, hyperexcitability and convulsions, slow, irregular pulse, becoming rapid before death, and paralysis of the vagi) were observed. This leaves little room for doubt that, in high concentrations, dichlorethylsulphide is absorbed through the lungs and produced its characteristic effects upon the body.

EXPERIMENT 16.—Dog V12, male; weight, 11.4 kilos.

March 21.

10.15. Pulse 168, respiration 36. Very active and playful.

10.30-11.30. In gassing chamber, exposed to 0.3 mgm. per liter of dichlorethyl-sulphide—restless, rapid respiration, excitement, salivation, vomiting.

11.40. Hyperexcitable. Coughing.

11.50. Pulse 108, respiration 56.

1.00. Defecates. Marked muscular weakness, ataxia.

1.25. Convulsions.

1.45. Pulse 152, respiration 50.

3.30. Pulse 168, respiration 64; marked muscular weakness; salivation.

4.00. Vomits.

4.30. Pulse 176, respiration 52, pulse becoming feeble. Killed with ether.

Autopsy.—Mouth, esophagus, and stomach normal; duodenum shows congestion, contents bloody; small intestine has congested areas of mucosa; trachea, some slight membrane; lungs, one lobe congested and emphysematous; heart, kidneys, liver, and spleen, normal.

EXPERIMENT 17.—Dog V13, female; weight, 13.5 kilos.

10.00. Pulse 96, respiration 26.

10.05–11.05. In gassing chamber, exposed to 0.28 mgm. per liter of dichloroethylsulphide. Excitement, irritation of upper respiratory tract, salivation, and vomiting.

11.08. Loose stools.

11.35. Pulse 44, respiration 96; pulse irregular, expiration spasmodic.

12.35. Pulse 44, respiration 60; diarrhea, salivation, hyperexcitability with typical convulsions.

1.20. More violent convulsions.

2.05. Pulse 68, respiration 28. Animal very weak.

2.30. Vomits voluminous, foamy fluid. Bloody diarrhea.

3.40. Pulse 70, respiration 30. Very weak, but still struggles some.

4.00. Killed with ether.

Autopsy.—Trachea slightly congested, contains some fluid; lungs, one lobe shows slight hemorrhage, few patches of emphysema; esophagus and stomach normal; upper intestinal tract deeply congested, congestion decreases until in ileum, normal; large intestine congested.

FATE OF DICHLORETHYLSULPHIDE IN THE BODY

Further convincing proof of the absorption of the sulphide through the lungs was furnished by the detection of one of the products of hydrolysis, dihydroxyethylsulphide, in the urine of animals poisoned by dichloroethylsulphide by inhalation. This hydrolytic product could also be found in the urine after the injection of mustard gas.

Dihydroxyethylsulphide was injected into a dog, the urine collected and examined for this substance. A positive test was obtained. Urine from a normal dog failed to give a positive reaction. This was necessary because of the occurrence of ethylsulphide and its precursors in normal dog's urine. This proves that the substance was excreted, in part at least, unchanged. The injection of dichloroethylsulphide was next tried, and the urine found to contain the dihydroxyethylsulphide. The inhalation experiments were then performed.

EXPERIMENT 18.—Dog V47, female; weight, 13.2 kilos.

May 19. Intravenous injection of 100 mgm. per kilo of dihydroxyethylsulphide in 10 c. c. saline.

May 20. No urine passed in cage; 230 c. c. urine by catheter. This was evaporated under diminished pressure to small volume, 25 c. c. of concentrated hydrochloric acid was added, and distillation carried out under diminished pressure. The distillate was extracted with ether, and the extract evaporated. The residue was tested by applying small amounts to the skin of several individuals. A typical mustard-gas reaction developed. This was considered evidence of the presence of dichloroethylsulphide.

EXPERIMENT 19.—Dog V49, female; weight, 21.4 kilos.

May 20–21. Over a period of 24 hours, injected subcutaneously with 60 mgm. per kilo of dichloroethylsulphide in olive oil, 10 mgm. per kilo at a time. Immediately after last injection, dog was catheterized and 200 c. c. urine obtained. This was concentrated as above, and tested for dichloroethylsulphide by applying to the skin of several men. No reaction obtained. It was then treated as above, and a slight amount of oily substance obtained on the distillate. The distillate was extracted with ether, and the ether evaporated, leaving a globule of oil. This oil was placed in a small test tube, and the mouth of the tube held against the arm for 3 minutes. After 24 hours a distinct dichloroethylsulphide effect was obtained. The distillate contained mustard gas, and the urine dihydroxyethylsulphide.

EXPERIMENT 20.—Dog V54.

May 24.

10.25–10.55. Gassed in continuous flow chamber for 30 minutes, 0.52 mgm. per liter.

May 25.

9.00. Pulse 102, respiration 34. Great muscular weakness. Unobserved, but seems to have been in convulsions.

10.00. Urine taken with catheter and examined for dihydroxyethylsulphide.

10.07. Dog dies in coma.

A severe reaction from the re-chlorinated product was not obtained, but a sufficient reaction was obtained to furnish evidence of dichlorethylsulphide being present.

It was found possible by the application of 0.1 to 0.2 gram per kilo to the skin of dogs to obtain the characteristic effects of the absorption of mustard gas; salivation; vomiting; diarrhea; hyperexcitability; rapid, feeble pulse and depression, but neither convulsions nor slowing of the heart. The product of hydrolysis of mustard gas was also detected in the urine.

EXPERIMENT 21.—Dog V90; weight, 16 kilos.

11.00. Normal pulse 108, respiration 36. Chest and abdomen shaved; 1.6 grams of pure dichlorethylsulphide rubbed into skin with glass rod. Animal placed so that draft prevented absorption by inhalation of the vapors.

11.30. Second application; 1.6 grams rubbed in (total quantity, about 200 mgm. per kilo).

12.00. Pulse 96, respiration 150.

1.40. Pulse 138, respiration panting.

5.00. Pulse 168, respiration panting. Dog placed in clean metabolism cage.

June 4.

9.00. 200 c. c. of urine collected overnight; examined for dihydroxyethylsulphide. Positive findings. Pulse 198, respiration 36. Dog depressed; slight salivation.

June 5.

9.00. Pulse 186, respiration 48. Dog etherized.

MECHANISM OF ACTION

TOXICITY OF PRODUCTS OF HYDROLYSIS

The latent period in the development of the effects of dichlorethylsulphide, either local upon the eyes, skin, or respiratory tract, or systemic upon the heart, nervous system, and digestive tracts, suggests that the substance may be altered in the body before exhibiting its characteristic actions. In fact, the absence of any immediate effects when the aqueous solution was injected directly into the blood stream makes this assumption almost imperative. The simplest chemical change which this substance undergoes in vitro is hydrolysis into hydrochloric and dihydroxyethylsulphide. That this change takes place in the animal organism was shown by the detection of dihydroxyethylsulphide in the urine. However, an injection of a hydrolyzed solution of dichlorethylsulphide was without effect. The dihydroxyethylsulphide, when applied pure to skin of man and dogs, produced no irritation whatever.^c As much as 0.3 gram per kilo was injected intravenously into a dog without producing any apparent effect, immediate or remote. An injection of 1,400 mgm. per kilo caused only a slight stupor and loss of coordination, with a quick return to normal, and none of the symptoms of the dichlorethylsulphide were present.

^c Victor Meyer states that this substance is nontoxic. *Berichte der deutschen chemischer Gesellschaft*, Berlin, 1886, xix, No. 3, 3259.

EXPERIMENT 22.—Dog EM575, male; weight, 7.8 kilos.

November 18.

2.30. Normal pulse 80, respiration 20.

2.45. Intravenous injection of 1,400 mgm. per kilo of dihydroxyethylsulphide in 100 c. c. of water (total, 10,920 grams). Injection followed by salivation and slight nausea.

2.50. Dog shows slight ataxia. Pulse 120, respiration 20.

3.10. Pulse 110, respiration 20.

3.50. Pulse 110, respiration 20. Dog appears stupid, and exhibits a slight ataxia similar to light alcohol poisoning. No serious symptoms apparent.

5.00. Pulse 105, respiration 20. Dog quiet, perhaps slightly depressed. Eats and drinks with indifference.

November 19.

9.00. Dog normal. Pulse 98, respiration 24.

November 20.

9.00. Dog normal. Pulse 105, respiration 30.

EXPERIMENT 23.—Dog EM576; weight, 5.9 kilos.

November 19.

10.30. Normal pulse 100, respiration 20.

10.45. Intravenous injection of 200 mgm. per kilo (total, 1,200 mgm.). Dihydroxyethylsulphide in 50 c. c. of water. Animal exhibited no symptoms whatever. Observed for three days.

EXPERIMENT 24.—The pure dihydroxyethylsulphide was rubbed into the skin on four dogs and five men and produced no irritation, either immediate or remote.

This product of hydrolysis is not responsible for the effects of mustard gas. The other product of hydrolysis is hydrochloric acid and is not a very toxic substance. Relatively large amounts can be injected intravenously without producing any marked effect. This is readily understood. When injected intravenously it is immediately neutralized by the "buffer" action of the blood. The blood does not become acid and the tissues are never really exposed to the acid. When strong solutions are placed on the skin or mucous surfaces, or injected into the tissues, an irritating effect is noticed. Hydrochloric acid, however, injected in very large doses, does produce very definite effects upon the animal and can cause death. Both products of hydrolysis of mustard gas are very readily soluble in water and very sparingly soluble in organic solvents, or, in other words, have a low lipid solubility or partition coefficient. It would be expected from this that they would not readily penetrate cells. Harvey has shown this to be true for hydrochloric acid.¹

THEORY OF ACTION

Dichlorethylsulphide is very slightly soluble in water and very freely soluble in organic solvents, or has a high lipid solubility or partition coefficient.^d It would therefore be expected to penetrate cells very readily. Its rapid powers of penetration are practically proven by its effects upon the skin. Having penetrated within the living cell, it would undoubtedly hydrolyze. The liberation of free hydrochloric acid within the cell would produce serious effects and might account for the actions of dichlorethylsulphide. The mechanism of the action of dichlorethylsulphide may be summarized as follows: 1. Rapid penetration of the substance into the cell by virtue of its high lipid solubility. 2. Hydrolysis by the water within the cell, to form hydrochloric acid and dihydroxyethylsulphide. 3. The destructive effect of hydrochloric acid upon some part or mechanism of the cell.

^d Attempts to determine accurately the partition coefficient of this substance are unsuccessful, due to the rapidity with which it hydrolyzes. It appears to be over 200, using xylene and water at 20° C.

Although hydrochloric acid does not penetrate cells readily and is easily neutralized by the buffer action of the fluids of the body, one might expect by flooding the body with large quantities of acid to produce some of the characteristic effects of mustard gas. Stimulation of the respiratory center is a well-known effect of acid. Convulsions and salivation may be produced by injection of hydrochloric acid and it was found possible to produce slowing of the heart by rapid injection of this acid.

The delayed action of mustard gas may be explained by the formation of some compound with some constituent of the blood. However, blood taken from dogs which had been poisoned with mustard gas and were exhibiting typical symptoms at the time injected into normal dogs, produced no effect. Serum treated in vitro with mustard gas and allowed to stand and then injected into a dog produced no effect. The fluid which is formed in the vesicles and blebs produced by the application of mustard gas to the skin produces no mustard-gas effects.

EFFECTS OF ADMINISTRATION OF SODIUM BICARBONATE

By the administration of large quantities of sodium bicarbonate, both intravenously and by mouth, the symptoms following an intravenous injection of dichlorethylsulphide could be delayed, and convulsions, but not death, were prevented.

Ten cubic centimeters per kilo of the fresh, aqueous mustard-gas solution given intravenously always caused convulsions, violent other symptoms, and death. A series of 11 dogs injected with this dose of the solution, were treated with 10 c. c. per kilo of 5 per cent sodium bicarbonate by mouth and intravenously every hour for five or six hours. In one of these animals no benefit was obtained; in 6, symptoms were delayed and milder; in 4, convulsions were prevented. Death was never prevented, although sometimes apparently delayed. The action of mustard gas on the heart appeared to be increased, and most of the animals showed a very slow, failing heart before death. Since sodium bicarbonate (Harvey) is known to penetrate cells only with difficulty, much benefit was not expected. Numerous amines, especially those of high lipid solubility, have been tried, but thus far the effects have not been consistent. A substance possessing the same physical properties as mustard gas, but slowly yielding alkali on hydrolysis, would be ideal to try for treatment.

EFFECT OF TEMPERATURE ON TOXICITY

The fact that the velocity of hydrolysis of dichlorethylsulphide is very much decreased by lowering the temperature, suggested trying the effects on animals at a high and low temperature. The influence of temperature was quite marked on drugs which underwent a change in the body before acting. The lethal dose of atoxyl and colchicine was increased markedly for frogs when the temperature was lowered, and decreased when it was raised to 37° C.² Atoxyl is supposed to be reduced in the body before acting and colchicine is oxidized. According to the theory which has been advanced for the mode of action, one might expect that at a low temperature the rate of liberation of hydrochloric acid in the cell might be slow enough to be nontoxic, for a dose which would prove fatal at a higher temperature.

Fish were used for the experiments. Those kept at a low temperature survived the same dosage which proved fatal to those kept at room temperature.

EXPERIMENT 25.—Seventeen healthy catfish were exposed, in groups of four to six, to dichlorethylsulphide by immersing in a quarter saturated solution of mustard gas in tap water at 10° C. for five minutes. Ten of these were placed in water at room temperature (24° to 26° C.), and ten died (100 per cent) within 28 hours. The other seven fish were kept at 8° to 10° C., and one died in 96 and another in 108 hours, while the other five survived for 5 days, when observations were discontinued.

EXPERIMENT 26.—Fifteen goldfish were exposed, as in experiment 25, to a half-saturated solution for 10 minutes. Eight were transferred to a bath at room temperature (25° C.) and seven to a bath at 8° to 10° C. Of the first group, four died in 26 hours, two died in 56 hours, and two died in 6 days. Of the second group, all survived 17 days, when observations were discontinued.

It is quite noticeable that in the catfish which were kept at room temperature hemorrhages generally developed in the fins and tails and in the ventral surface of the body after 16 to 20 hours,^e while in those kept cold, no hemorrhage was ever observed. Symptoms, which were marked in the first group, were never observed in the second.

Although this evidence fits in perfectly with our theory, it is well known that the effect of drugs is changed by decreasing temperature.^f The following experiments indicated that hydrochloric acid was toxic for fish whether the fish were cooled after exposure or kept at room temperature.

EXPERIMENT 27.—Eight catfish were exposed to 0.05 per cent hydrochloric acid for five minutes. Four were placed at room temperature (25° C.), and four placed at 8° to 10° C. Of the first group, all died within 40 minutes; of the second, three died within 30 minutes, and one in 150 minutes.

EXPERIMENT 28.—Sixteen goldfish were exposed in the same manner as in experiment 27. Eight were kept at room temperature (20° C.) and eight at 8° to 10° C. Of the first group two died in 1 hour, and six in 1 hour and 20 minutes. Of the second group all died within 1 hour.

An experiment on atropine and one on sodium cyanide indicated that these substances were just as toxic for fish whether they were kept at ordinary temperature or cooled, after exposure.

EXPERIMENT 29.—Four goldfish were exposed for 10 minutes to 0.01 per cent atropine sulphate solution. Two were placed in a bath at 8° to 10° C. In the first group, both died in 6 to 7 hours; in the second group, both died in 5 to 7 hours.

EXPERIMENT 30.—Six goldfish were exposed for 10 minutes to 0.48 per cent solution of sodium cyanide. Three were kept at 20° C. and three at 8° to 10° C. They died in 3, 5, and 8 hours, and 4, 6, and 8 hours, respectively.

Catfish survived fifteen times the concentration of hydrochloric acid present at the end of 5 minutes in the half-saturated water solution of mustard gas, and three times the concentration present at the end of 24 hours. Fish survived 15 minutes' exposure in this solution after it had stood 1 hour at room temperature.

It is evident that these experiments on fish tend to substantiate the theory of intracellular liberation of acid.

^e It is interesting to note that dichlorethylsulphide appears to act on the skin of catfish and not that of goldfish.

^f Sollman (A Manual of Pharmacology, 1917, 94) holds that digitalis, veratrin, nicotine, strychnine, tetanus toxin, chloral, and alcohol are rendered more active, morphine and curare less active, by raising the temperature for cold-blooded animals.

PROPERTIES AND ACTION OF SOME COMPOUNDS RELATED TO
DICHLORETHYLSULPHIDE

Various compounds related to mustard gas were prepared at one time or another by the offense chemical section of the Chemical Warfare Service. A cursory survey of their lipid solubility, rates of hydrolysis, and pharmacological effects was made.

The lipid solubility was estimated by using xylene and water. Victor Meyer³ noted that ethylsulphide was inactive, while the β -monochlorethylsulphide was less active than mustard gas. Monochlorethylsulphide and the two isomeric β - β -dichloropropylsulphides were all highly (though in different degree) lipid soluble and all hydrolyzed more or less rapidly in aqueous solution. All were active skin irritants, and more or less toxic on inhalation, producing lesions and symptoms comparable to those of mustard gas.

The theory of the intracellular liberation of hydrochloric acid as the mechanism of action of dichlorethylsulphide, explains all the experimental facts thus far observed. The histological changes in the skin have been stated to resemble hydrochloric acid burns. According to Warthin and Weller:⁴ "The lesion is a chemical burn unlike that produced by heat, electricity, or the ordinary corrosives such as sulphuric, nitric, and hydrochloric acids, or strong alkalis. Of all these agents, the effects are most closely allied to those of hydrochloric acid, but are much greater in intensity." Lillie, Clowes, and Chambers,⁵ in a study of the action of mustard gas on marine organisms, especially starfish eggs, have obtained evidence which supports our interpretation of the action of dichlorethylsulphide, *e. g.*, an intracellular liberation of hydrochloric acid as the toxic factor.

A theory to explain the "edema, fat, infiltration, multiple hemorrhages, and necrosis of the central portion of the liver lobule" by the "severe tissue effects by the halogen acids formed in the tissues" has been advanced by Graham⁶ for the delayed poisoning by chloroform and other alkyl halides. Graham's evidence is briefly as follows: Similar morphological changes can be produced especially in the liver by injection of hydrochloric acid into the portal vein. Sections of the chloroformed liver show an acid reaction with neutral red or Nile blue immediately, whereas such changes occur more slowly in the liver of normal animals after death. Carbon tetrachloride is more effective than chloroform and methylene chloride less effective in producing liver necrosis; this is in the same order as the amount of hydrochloric acid that can be liberated. Simultaneous injection of sodium carbonate with the chloroform anesthesia prevents or decreases the liver injury and other effects. Other alkyl halides give a typical morphological picture of chloroform poisoning. That these substances form halogen acids is shown by the excretion of the neutral salts in the urine. Chloral, which does not yield an appreciable quantity of hydrochloric acid in metabolism, does not produce these changes. While Graham did not discuss the question of how the acid is formed, he suggested Nef's⁷ ideas of dissociation, forming bivalent carbon.

It is evident that the theory suggested in this chapter is somewhat different. Graham⁶ did not consider intracellular liberation of acid, and was dealing with substances which do not readily yield hydrochloric acid on contact with water, but must undergo relatively slower metabolic changes by the tissues. The effects of mustard gas are not similar to those of delayed chloroform poisoning and, moreover, chloroform is a substance of an entirely different order of toxicity.

It is not impossible to reconcile these two different types of poisoning as both being due to hydrochloric acid. Graham's suggestion that "the liver is an organ which most strikingly manifests the chloroform necrosis, and that this organ is also the site of a most active metabolism, harmonize well with this hydrochloric acid theory," may explain the difference. As stated above, chloroform must be slowly metabolized to produce hydrochloric acid. By oxidation chloroform yields phosgene and hydrochloric acid. Phosgene readily yields hydrochloric acid on hydrolysis.

One is inclined to agree with Graham's statement that the halogen acids are suggested to be important factors rather than the only factor involved. Other acids must play a part, and possibly other substances than acids are involved.⁶

With mustard gas and analogous compounds where the radical, other than the acid radical, is nontoxic, the entire responsibility can be laid to the intracellular production of acid. The question of cell penetration, as well as ease of hydrolysis and lipid solubility, has to be considered in dealing with a series of compounds.⁷

It is interesting to note that most of the war gases can readily yield a halogen acid by hydrolysis. Whether the intracellular liberation of acid will explain their relative toxicity must be decided by future work. Their partition coefficients, their rate of hydrolysis, their volatility and other physical chemical properties may explain the differences in localization and intensity of action. The facts which can be gathered from the literature concerning dimethylsulphate, seem to indicate that its toxic action may be due to the intracellular liberation of sulphuric acid. The symptoms recorded in the literature due to this poison are very suggestive of mustard-gas poisoning—local redness and edema, generalized toxic and clonic convulsions, coma and death.⁸ The effect on the eyes⁹ and the clinical descriptions of several factory cases of poisoning resemble mustard gas¹⁰. Both Weber⁸ and Michiels,⁸ who worked experimentally on animals with this substance, discuss the possibility of the effects being due to acid poisoning. They decide against it because the amount of acid liberated is too small, the blood gases of the poisoned animal were found normal, sodium carbonate did not help poisoned animals, and it is doubtful whether time elapsed for a toxic dose to hydrolyze. Michiels found, moreover, that serum treated with a toxic dose of dimethylsulphide, incubated and injected into a rabbit, was nontoxic. So he agreed with Weber that the molecule is toxic and not a decomposition product. The evidence appears to be very suggestive for an intracellular liberation of sulphuric acid as the toxic factor. It was found that the partition coefficient is about 1.9, using xylene and water at 20° C., and that this substance hydrolyzes much more slowly than dichlorethylsulphide. It would be expected that the toxicity on intravenous injection would be less than mustard gas. Preliminary experiments indicate that 50 mgm. per kilo are necessary to produce the same symptoms as are given by 6 mgm. per kilo of dichlorethylsulphide. The symptoms appeared much more quickly in the case of the dimethylsulphate. This would indicate that mustard gas is prevented for a time from hydrolysis by being held in lipoids, while dimethylsulphate, having a much lower partition coefficient, is more readily transferred to an aqueous phase for hydrolysis. Certain facts noted later as having been observed with respect to the action of dichlorethylsulphide on the skin also led to this conclusion.

SUMMARY

The results of the experimental work which has been considered may be summarized as follows:

1. Dichlorethylsulphide is absorbed through the lungs and produces definite, characteristic, systemic effects.

2. The symptoms of injection of the substance are salivation, vomiting and diarrhea, tonic and clonic convulsions, slow and irregular heart, followed by a rapid pulse, and stimulation of the respiration.

3. A dose of six milligrams or less per kilo, injected intravenously in aqueous solution, proves fatal for dogs.

4. Dichlorethylsulphide appears to be excreted in the urine, in part at least, as dihydroxyethylsulphide, which has been shown to be a comparatively nontoxic body.

5. The lesions in the intestine suggest that excretion of the substance may also take place here.

6. The dichlorethylsulphide penetrates the cells, and in the aqueous phase of the cell, hydrolyzes to hydrochloric acid which is responsible for the damage.

7. Sodium bicarbonate in large doses somewhat alleviates the symptoms, but does not prevent death.

8. Fish are much less susceptible to this substance when kept at a low temperature after exposure rather than at room temperature. The hydrolysis of the substance is much slower at a low temperature.

9. Monochlorethylsulphide, and dichlorpropylsulphide are lipoid soluble and easily hydrolyzed. Both act similarly to mustard gas.

10. The evidence leads to the view that dimethylsulphate acts by intracellular liberation of sulphuric acid.

EFFECTS ON THE SKIN

INDIVIDUAL SUSCEPTIBILITY

Every investigator who has worked with dichlorethylsulphide has noticed that some individuals are much more susceptible to the substance than others. Victor Meyer, its discoverer, noted that his laboratory assistant was greatly affected by exposure to this agent, while he himself was not.¹¹ Similar observations have been made by many workers in laboratories. Despite the great differences in susceptibility, it is very improbable that any man or beast is immune to the action of mustard gas. It was possible to demonstrate beyond a doubt the individual variation in susceptibility, and methods were evolved by which determinations of susceptibility could be made.

METHODS

Two methods were used for determining the cutaneous sensitivity of individuals to dichlorethylsulphide. The first of these methods consisted in exposing skin to the vapors of the substance under constant conditions and determining the minimum time of exposure which was necessary to produce a visible reaction within 24 hours. The apparatus which was used in this method consisted of a small test tube (1 cm. by 10 cm.) containing a cotton plug saturated with pure dichlorethylsulphide held by means of a rubber stopper in a larger test tube which was filled with water. When not in use the smaller

tube was closed with a cork stopper. On being first prepared the tubes were allowed to stand unstoppered for about 24 hours in order to remove any volatile impurities that might be present. Before use the whole apparatus was placed in a constant temperature water-bath. In all this work 20° C. was taken as a constant-temperature for making exposures. The skin was exposed to the vapors in the smaller tube by holding the mouth of the tube firmly against the skin. Exposures were made for different lengths of time in order to determine the shortest exposure which would just produce a visible reaction, the minimum burning time. The reaction was not visible for some hours, and was noted 24 hours later. The reaction consisted in a circular area of erythema which was usually uniform. In certain cases a group of small, red spots might be all that was noticed. Longer exposure than the minimal gave rise to edema as well as erythema, and a still longer one to subsequent small vesicles or a well-defined blister over the entire area exposed. In this method the skin was exposed to supposedly saturated vapor at 20° C.

The second method which was used for studying the sensitivity of individuals consisted in applying to the skin standard solutions of mustard gas in paraffin oil. For most purposes the best solutions were a 1 per cent (1 gram of pure dichlorethylsulphide in 100 c. c. of oil), a 0.1 per cent and 0.01 per cent. A small drop of each of these solutions was applied to the skin of the forearm and the arm allowed to remain uncovered for about 10 minutes. The presence or absence of a positive reaction was indicated by the appearance or absence of erythema 24 hours later.

Within certain limits the amount of the solution of a given concentration of mustard gas which was applied to the forearm made no difference in determining whether the reaction was positive or negative. It made a difference in the intensity of the burn, a large amount of 1 per cent solution causing a blister, while one-tenth the quantity did not. For this reason it was advisable not to employ too large a quantity of the stronger solutions in making the test. The following experiments were made, applying at the same time the amount of solution of mustard gas in paraffin oil left on a glass rod after dipping it in the solution and shaking it off, and then applying about ten times the quantity. The reaction from the larger quantity is given in brackets. (Tables 28 and 29.)

TABLE 28.—*Irritating effects of dichlorethylsulphide applied locally*

Subject	Per cent solutions						
	1	0.1	0.08	0.06	0.04	0.02	0.01
H.....	—(—)	—	—	—	—	—	—
F.....	×	—(—)	—	—	—	—	—
C.....	—	—(—)	—	—	—	—	—
Hu.....	×	—(—)	—	—	—	—	—
T. K.....	—(—)	—	—	—	—	—	—
B.....	×(×)	—	—	—	—	—	—
M.....	×(×)	—	—	—	—	—	—
F.....	—	—(—)	—(—)	—	—	—	0
C. I. R.....	—	—(—)	—	—	—	—	—
C. I. R.....	×	—(—)	—	—	—	—	—
D. J. B.....	×	—(—)	—	—	—	—	—
D. J. B.....	×	—(—)	—	—	—	—	—
L. H. S.....	0	×	×	×	×	×	—
C. L. H.....	0	×	×	×	×	×	—
P. S. B.....	0	×	×	×	×	×	—
P. S. B.....	0	×	×	×	×	×	—
J. W. W.....	0	×	×	×	×	×	—
J. W. W.....	0	×	×	×	×	×	—
H. W. S.....	0	0	0	×	×	×	—
E. K. M.....	0	0	0	0	×	×	×

NOTE.—× indicates positive reaction; — indicates negative reaction; 0 indicates no solution applied.

TABLE 29.—*Irritating effects of dichlorethylsulphide applied locally*

Subject	Time read (hours)	1 per cent	0.1 per cent	0.01 per cent
S.....	24	X	—	—
N.....	48	X	—	—
N.....	24	X	—?	—
N.....	48	X	X	—
F.....	24	X	—	—
F.....	48	X	—	—
K.....	24	X	—	—
K.....	48	X	—	—
S.....	24	X	—	—
S.....	48	X	—	—
C. U.....	24	X	—	—
C. U.....	48	X	—	—
W.....	24	X	X	—
W.....	48	X	X	—
F.....	24	X	X	—
F.....	48	X	X	—
D.....	24	X	X	—
D.....	48	X	X	—
L.....	24	X	X	—
L.....	48	X	X	—
Su.....	24	—	—	—
Su.....	48	—	—	—

The question has been raised as to what length of exposure was given to the oil solution on the arm. Within 5 minutes, where only a small amount of solution was left on, absorption or evaporation was complete. When a larger amount of solution was applied, rubbing off the excess 5 minutes after application made no difference in whether the reaction was positive or negative. When the test was applied the subject left the sleeve rolled up for about 10 minutes and then continued his usual duty.

Twenty-four hours after making the test was a convenient time for reading the results. The following figures show that any time between 24 to 48 gave the same result. Less than 24 hours' readings should not be taken as some individuals were rather slow in reacting.

Paraffin oil was chosen as the solvent for making the test, for the following reasons: It was not very volatile; the solution of mustard gas in it was fairly stable; it did not spread greatly when applied to the skin; and it was probably not readily absorbed. Mustard-gas vapor was given off, however, from a 1 per cent solution in paraffin oil. A small amount of this solution placed in a test-tube and held against the skin of a sensitive individual (for 10 minutes) caused erythema. Solutions of mustard gas in other solvents than paraffin oil were tried on a selective number of individuals of the resistant, average, and sensitive types. The solvents used were linseed oil, cottonseed oil, kerosene, absolute alcohol, and paraffin oil as a control. The solution in absolute alcohol was the more reactive, while those in linseed, cottonseed, and kerosene oils were less reactive than that in paraffin oil. The greater reactivity in alcohol was probably due to its volatility leaving a stronger solution on the skin a few seconds after it was applied.

The skin of different parts of the body probably reacted slightly differently from mustard gas, although this was not tested fully. The solutions were always placed on the inner surface of the forearm. One point which is to be noted is that areas of skin in the neighborhood of old mustard-gas burns were more sensitive than other areas. They should be avoided in making the test.

The first method undoubtedly gave the most accurate results, although the second was very much simpler and more rapid in its application. Numer-

ous tests were made on individuals by these methods in order to determine if each method gave the same result. Men who were sensitive to one test were sensitive to the other, and vice versa. Roughly, it may be said that a man who gave a reaction to the 0.01 per cent solution would show a reaction from a 15-second (or less) vapor exposure, while a man who showed no reaction to the 1 per cent solution would be negative or only faintly positive to a 4-minute vapor exposure.

A method such as the second method described above might be applicable in the field or factory, being used to detect individuals who are especially sensitive to mustard gas so that they may be removed from areas which are exposed to this gas. It would be an easy matter to examine thousands of men and determine quickly which ones were especially susceptible to the gas and which were less susceptible. A sensitive individual living in a region where mustard gas is present is practically certain to be a casualty. It would be far easier to remove him before injury. This idea may sound very impractical, but it does not seem less practical than applying ointments to the body for protection.

RESULTS OF VAPOR METHOD

This method was applied to only a few individuals working around the laboratory. The results are shown in Table 30.

TABLE 30.—*Time of exposure to vapor tests required to produce a visible reaction*

Subject	Time	Subject	Time	Subject	Time
	<i>Seconds</i>		<i>Minutes</i>		<i>Minutes</i>
H. C. J.	1	V. L.	1	— B.	4
J. A.	5	— F.	1	R. H.	4
H. P.	5	H. W.	1	— G.	4
L. D. S.	5	— R.	1	C. I. R.	4
W. V. C.	10	L. S.	1	— P.	4
H. W. S.	15	— C.	1	P. J. H.	4
E. K. M.	15	F. W. F.	1	F. W. S.	5
J. W. W.	15	— W.	1	G. L. S.	5
C. L. H.	15	La P.	1	R. A. T.	5
C. H.	15	— K.	2	— B.	5
— H.	30	— Y.	2	— K.	7
— N.	30	— L.	2	M. R. T.	10
R. E. W.	30	G. A. D.	2	— B. (colored)	10
— P.	30	— L.	3	C. B. (colored)	10
— A.	30	— D.	3	C. W. B. (colored)	10
A. W. K.	30	— S.	3	O. H. (colored)	10
A. C. S.	30	H. L. I.	3	H. B. (colored)	10
H. H. C.	30	C. B. M.	3	W. M. L. (colored)	10
	1	C. F. W.	3		

It is interesting to note that the very extreme cases had a minimum burning time of 1 second and 10 minutes, respectively. In other words, it may be stated roughly that one of these individuals was six hundred times as sensitive as the other. The man who gave a reaction from a 1-second exposure blistered from a 5-second exposure, or one to which the vast majority of individuals will give no reaction. When first found this subject blistered from the application of the 0.01 per cent solution in paraffin oil. Fortunately, it was possible to obtain a complete history and physical examination, but nothing of note was found. This man had never been exposed to mustard gas nor had he received even a small experimental burn when first tested.

RESULTS OF TESTS WITH OIL SOLUTIONS

As has been pointed out, the oil-solution method of determining sensitivity was very much easier and more rapid in its application than the ~~vapor-test~~

method. Results were obtained on rather large groups of individuals, using this method. Table 31 summarizes the results obtained on a group of men at the American University Experiment Station. Practically all these men were indoor workers, and a great many of them had been more or less exposed to mustard gas.

TABLE 31.—*Skin irritation from local application of dichlorethylsulphide*

Reaction			Number of men	Percent- age of total
1 per cent	0.1 per cent	0.01 per cent		
Positive.....	Positive.....	Positive.....	7	2.0
Do.....	do.....	Negative.....	26	7.5
Negative.....	Negative.....	do.....	238	68.6
.....	do.....	do.....	76	21.9
Total.....	347	100.0

A similar test on a larger scale was carried out at the Edgewood Arsenal, Edgewood, Md. This was done to determine: (1) In a large group of men, the relative number of hypersensitive, average, and resistant individuals. (2) If among factory workers in mustard, the hypersensitive individuals were those most frequently burned, and the resistant those seldom burned.

The method of conducting the test was to treat each man on the forearm with a 1 per cent and 0.01 per cent solution of mustard gas in paraffin oil. Twenty-four hours later the man was examined for a positive or negative reaction to these solutions (indicated by the presence or absence of visible erythema). In a group of 915 men, the actual time for 6 workers to apply the solutions was about 10 minutes, and to read the tests the next day about 20 to 25 minutes, including taking the names of the hypersensitive men.

Table 32 indicates the relative number of resistant, average, and hypersensitive individuals.

TABLE 32.—*Effect in individuals of local application of dichlorethylsulphide*

Reaction		Class	Number of men	Per cent of total
1 per cent	0.1 per cent			
Positive.....	Positive.....	Hypersensitive.....	43	3.3
Do.....	Negative.....	Average.....	709	55.3
Negative.....	do.....	Resistant.....	530	41.4
Total.....	1,282	100.0

The number of men available for testing the second proposition was too small to arrive at definite conclusions (only 31 men from the mustard-gas plant were present). Tests were also made on 51 hospital cases suffering from eye or skin effects of mustard gas. It was evident from these that average and resistant men were frequently burned. An examination into conditions at the plant showed that most of the casualties had occurred in cleaning pipes and where breakage occurred, under conditions where any man would be burned. Any individual will be burned from the application of the liquid to the skin or from a high enough vapor concentration. It was true, however, that where a sensitive and a resistant individual were burned under the same conditions the sensitive one had the more severe burn and required longer treatment.

In cases of relatively long exposure to vapor of fairly low concentration, it is certain that conditions will arise where hypersensitive men will be burned severely enough to become casualties, while resistant and average individuals will escape without burns or only slight ones.

Table 33 is the result of a test made on negroes. The few of these previously examined by the vapor test had been found very resistant. Only the 1 per cent and 0.1 per cent solutions were used.

TABLE 33.—*Sensitivity of negroes to dichlorethylsulphide*

Reaction		Number of men	Percentage of total
1 per cent	0.1 per cent		
Positive.....	Positive.....	0	0.0
Do.....	Negative.....	13	15.0
Questionable.....	do.....	6	7.0
Negative.....	do.....	65	78.0
Total.....		84	100.0

It is seen from Table 33 that negroes as a race have a much more resistant skin than white men. No negro of the 84 examined reacted to the 0.1 per cent solution, and of course none would react to a more dilute one. About 10 per cent of white men reacted to the 0.1 per cent solution, while 2 to 3 per cent reacted to the 0.01 per cent solution, or were hypersensitive. About 78 per cent of the negroes failed to react to the 1 per cent solution, while only 20 to 40 per cent of the white men did not show a reaction.

VARIATIONS IN SUSCEPTIBILITY IN THE SAME INDIVIDUAL

In the above discussion it has been tacitly assumed that the sensitiveness of a single individual is always the same. Such is not the case. The sensitiveness of a single individual is the same from day to day provided all conditions are the same, but may vary greatly under different conditions—the physiological variation in sensitiveness of the individual.

In order to show that the sensitiveness of the individual does not vary from day to day under the same conditions, a number of determinations of susceptibility were made upon the same individual on successive weeks. These determinations showed that the sensitiveness of an individual did not vary greatly, probably less than 25 per cent from day to day. An individual who was positive to a 15-second exposure on one day could be negative to 15 seconds but positive to 30 seconds a week later. He was never negative to a 1 or 2-minute exposure. Also, an individual who was negative to a 4-minute burn and positive to a 5-minute burn at one time could be negative to a 3-minute burn and positive to a 4-minute burn a week later, but he would not react to a 1 or 2-minute burn. So constant, in fact, was the sensitiveness of an individual that it was possible to plot a curve of the least time required to produce a burn (erythema) at different concentrations. If the variations in sensitiveness from day to day had been great, it would have been impossible to plot these curves, and there would have been many burns on the wrong side of the curve, and many negatives on the other side.

There are undoubtedly many conditions which influence the sensitiveness of the individual to mustard gas, but of these only two have been thoroughly investigated; sweating and moisture. A number of individuals from the laboratory were selected and given burns upon the forearm of different lengths of time, from 1 minute to 5 minutes, according to the known sensitiveness of the individual. A very mild burn was desired. The method used for burning was the "standard test-tube vapor test." The individual was then instructed to go out and run until the whole body, including the forearm, was in a profuse sweat. He was then given two other burns of the same length exposure, as before, one upon the moist, sweating arm, the other upon a part of the arm which was wiped dry with a towel. It was noted that in every case both of the burns made after exercising were distinctly more severe than those made before exercising, and the skin which was wiped dry usually received a more severe burn than the skin which was left moist. In another experiment performed in a similar way the feet of the subject were kept in a tub of hot water until the whole body was in a profuse sweat. The results were essentially the same. This action may have been due to the effect upon the sweat ducts, as it is known that the gas enters most readily these ducts. On the other hand, the action may have been due to the moisture. Experiments were carried out on the effect of moisture in the following way. An area of the forearm was kept moist for a few minutes with wet cotton. The sponge was then removed, and two vapor tests were made, one over the moist area and one over the normal dry skin. In the first three cases mild burns were given; in the last three cases, severe burns. The moist burn was always the more severe, in one case producing a blister when the other did not.

SUSCEPTIBILITY OF THE SKIN OF ANIMALS

The paraffin oil test was used on a number of animals and indicated that differences in susceptibility existed in different species and in different individuals of the same species. Table 34 shows the results.

TABLE 34.—*Susceptibility of skin of animals to dichlorethylsulphide*

Species	Number tested	Percentage positive to—		
		1 per cent	0.1 per cent	0.01 per cent
Horse.....	1	100	100	100
Dog.....	91	83	35	0
Ooat.....	11	55	36	0
Rat.....	10	30	20	0
Monsee.....	7	70	14	0
Rabbit.....	2	100	0	0
Guinea pig.....	12	33	0	0
Monkey.....	9	22	0	0

The horse appeared to be the most sensitive and the monkey and guinea pig the most resistant species, while the dog seemed to have a sensitivity as near man as any of the other species. However, the number of animals examined was too small for any far-reaching conclusions, and it is to be noted that no animal exhibited a reaction at all similar to that in man. No animal has yet been found which will give a blister from the application of mustard gas.

DISCUSSION

The only factor in the general characteristics of the skin which would appear to have a distinct bearing on the question of sensitivity is the apparent thickness of the skin. The fact that negroes as a race are much less susceptible to this substance than the white race furnishes a clue to the reason for susceptibility. Any constant differences in the skin of negroes and white men might furnish a basis for future work.

The following experiments tend to throw some light on the mechanism of absorption of mustard gas by the skin and, hence, on the question of susceptibility.

Fifteen minutes after pure dichlorethylsulphide was applied to the skin it could be almost entirely removed by long-continued rubbing with kerosene. This indicated that the substance was not immediately absorbed into the deeper layers of the skin. A resistant individual whose normal minimum burning time was 4 to 5 minutes and who did not react to the 1 per cent oil solution, could be made to give a reaction to a 15 to 30-second exposure or a 0.01 per cent oil solution by covering the area of application with a glass cup immediately after and leaving it covered for 6 to 8 hours.

It was found that when two vapor tests were made under identical conditions on the arm of a sensitive individual (5 minutes' exposure) and immediately after the exposure the arms of the two individuals were impressed on each of the exposed areas for 5 minutes, the burns were modified in intensity. If the recipients were respectively more or less resistant than the donor, that burn on the donor's arm given to the more resistant man was the mildest. This is very striking. If a sensitive individual impresses his arm alternately against burns of the same concentration and exposure on a resistant and sensitive man, the recipient receives a more severe burn from the sensitive than from the resistant man. This would indicate that the skin of a resistant individual displays a greater affinity or capacity for dichlorethylsulphide than that of a sensitive man. A tentative explanation of this phenomena can be made as follows: A three-phase system is involved—the air over the skin surface constitutes the outer phase; some fatty or keratinous elements of the skin the central phase; and a cellular portion of the skin the inner phase. The central phase is rich in lipoids and poor in water, while the inner phase is rich in water and poor in lipoids. After exposure to the vapors of dichlorethylsulphide the central phase is the absorbing agent and tends to establish equilibrium with the other two phases. On account of the lipid nature of the central phase no damage is produced here because the compound is not hydrolyzed. On its passage from the central to the inner phase, hydrolysis takes place within the cell and damage results when a sufficient concentration of hydrochloric acid is attained. The outer phase is constantly being freed from vapor by diffusion and convection currents, so more and more can evaporate from the central phase. The susceptibility of an individual depends on the relative power of the central phase to hold the poison in an inactive form (not hydrolyzed) and prevent its entry into the inner phase at a sufficient velocity to result in the formation of a toxic concentration. No attempt was made to localize the central or inner phase with any definite structure of the skin. As mustard gas is known to penetrate the sebaceous ducts, the fat here might form one phase and the epithelial lining another.

PRACTICAL APPLICATION

Anyone who observes the tremendous difference between individuals is struck with the practical use that might be made of this difference. There are individuals who show distinct burns (erythema) from a 5-second exposure, while working beside them are men who require an exposure of 5 to 10 minutes to produce a burn. The hyperemia produced by the 5 seconds' exposure is not serious when limited to a small area, where it is closely surrounded by normal tissue, but a hyperemia of no greater intensity when produced over a large area of the body may make it imperative that this individual be relieved from duty. The edema and itching may be quite distressing, and prevent the patient from sleeping or resting. He may have to spend most of his time bathing the injured parts with cold water to get relief. The man beside him, however, may be exposed to the same concentration for 10 to 50 times as long and show absolutely no effect. The former individual should not be allowed to work in any region where there is even a low concentration of mustard gas, for if he does he is certain to be burned severely, and practically certain to become a casualty. The latter individual, on the other hand, would make a splendid workman in a mustard-gas factory or a splendid soldier in a territory which has been shelled with mustard gas, if provided with a mask.

The following suggestions appear warranted from this investigation in sensitivity to mustard gas:

1. Sensitivity tests should be made routine in all plants handling mustard gas, and only the more resistant individuals should be stationed there if possible. Application of a single solution is all that is necessary. The 1 per cent solution will give about 40 per cent of the total men examined to be used in mustard gas. If a larger percentage is desired, lower percentage (0.5 per cent) solution can be substituted.

2. The feasibility of withdrawing the hypersensitive men from the line from any duty where mustard gas may be encountered should be considered. This would involve about 3 per cent of the men. The actual carrying out of sensitivity tests would be very simple—the application of a 0.01 per cent solution of mustard gas in paraffin oil to the forearm of each man and the observation of this spot 24 to 36 hours later. The time required would be much shorter than that necessary for venereal inspection of a company. The hypersensitive men are certain to become casualties if exposed to mustard vapor even in low concentrations, and in this way be eliminated afterwards if not before.

MECHANISM OF ABSORPTION BY THE SKIN

CHANNELS OF ABSORPTION

At an early stage in these investigations it was observed that after exposure of the skin to either the liquid or vapor the most efficient method of removal was washing with some solvent of low volatility, such as kerosene, followed by thorough rinsing with soap and water. With such a treatment it was found possible to apply the oil to the skin and by washing after 2 or 3 minutes to either prevent the subsequent delayed reaction entirely or to reduce it to a slight hyperemia. The very narrow time limits within which these preventive measures were effective indicated a remarkably rapid absorption of at least a

part of the gas. It was found, however, that if the sponging with kerosene was continued vigorously for 20 to 30 minutes, with frequent renewals of both sponge and solvent, vesication could be prevented in most cases after an exposure of 10 minutes or less and in rare instances after 15 minutes. (Table 35.)

TABLE 35.—*Removal of dichlorethylsulphide from skin by washing with kerosene*

Subject	Length of exposure	Kerosene treatment	Degree of burn after 24 hours
	<i>Minutes</i>	<i>Minutes</i>	
B. E.	10	10	++++
A. H.	10	10	+++
E. W.	10	10	++
P. E.	10	15	+++
H. A.	10	15	+++
E. C.	10	15	+++
M. C.	10	20	+
C. R.	10	20	++
E. C.	10	20	+
B. R.	20	30	+++
G. R.	20	30	+++
B. C.	30	30	+++
K. E.	90	60	++++
L. Y.	10	10	+++
L. Y.	10	30	+
H. E.	10	10	+++
H. E.	10	45	+

The following tests were made on the shaved and dried skin of the forearm by the "nailhead method." A nailhead 3 mm. in diameter was pressed firmly against filter paper saturated with dichlorethylsulphide and then applied with firm even pressure to the skin. After a definite period of time the exposed area was washed or "treated." This period of undisturbed contact between the oil and the skin (or, in subsequent experiments, between the vapors and the skin) will hereafter be referred to as the length of exposure. Since the reaction did not appear for several hours, and since the burns did not develop sufficiently to permit of accurate comparison in less than 24 hours, the first readings were made at the expiration of that period, and final readings after 48 hours. The reactions as observed at that time are graded as follows:

- + Mild erythema.
- ++ Moderate erythema and swelling.
- +++ Mild vesication with slight surrounding erythema.
- ++++ Severe vesication with slight surrounding erythema.
- +++++ Severe vesication with marked surrounding erythema and edema.

It should be noted in the table that +++ indicates the penetration of sufficient mustard gas to cause a blistering burn while + and ++ indicate that the amount of mustard gas introduced is insufficient to cause a blister, but only redness and slight swelling. Beyond the limits given above it is unsafe to make quantitative comparisons of two or more burns.

A 10-minute exposure, if washed with kerosene for 10 minutes or less, blistered; the actual blistering could be prevented in most cases by washing for 15 minutes or more. Little added benefit could be obtained by treating longer than 25 to 30 minutes. Where the time of exposure was increased to 15 minutes or more vesication could barely be prevented, even after rubbing or sponging for an hour.

That dichlorethylsulphide was actually being removed from the skin after the first few minutes of treatment was shown by the observation that unless the sponge and kerosene used were frequently changed, and the surrounding areas thoroughly washed, the resulting burn was greatly increased beyond the size of the original exposure—following in general the areas wet by kerosene—and in some cases even the operator's fingers became contaminated with the gas and a burn resulted.

Prolonged washing was tried with soap and water after 10 to 15 minutes in a similar manner; but though some benefit was observed, it was not nearly as marked as when the washing was done with kerosene or some solvent for the oil (vaseline, acetone, alcohol, and benzene were tried).

From these observations, it is quite evident that the dichlorethylsulphide was at first rapidly taken up by some element in—or adjacent to—the surface of the skin, and for 2 to 3 minutes it might be completely removed, and for 10 to 15 minutes partially removed, by prolonged washing with an organic solvent, and to a lesser extent with soap and water. This conclusion has been emphasized because it is an important consideration in dealing with the ultimate absorption of the substance.

In the absence of accurate information regarding the physical and chemical constitution of the outer layers of the epidermis and the exact location and condition of the mustard gas when first taken up, it appears inadvisable to speculate as to whether the gas is at first absorbed on the skin surface and then penetrates the sweat glands by capillary or absorption, or a mixture of both, or whether it passes to a certain extent directly through the cortical layers by a process of absorption or solid solution. Substances like keratin might be expected to absorb the compound and fats and lipoids to absorb or dissolve it. It is sufficient for the moment to consider the skin as a protective medium taking up the compound on its surface and offering a definite resistance to passage of the gas inward. This resistance may be gauged by determining the amount of gas which it is necessary to apply externally to insure the delivery to the inner tissues of a concentration sufficient to produce recognizable toxic effects. The nature of this resistance will become evident after the discussion of the loss of the gas from the skin by evaporation.

RELATION OF TIME OF EXPOSURE TO CONCENTRATION

It has been shown that individuals vary in their sensitivity to slight quantities of dichlorethylsulphide,¹¹ and a method for demonstrating this variation between individuals, by determining the shortest exposure to the vapors which will produce a visible reaction, has been described. Since any individual gives an increasingly severe reaction with increasing length of exposures until the full effects of the irritant are obtained (severe vesication), there should be a definite relationship between the concentration of the dichlorethylsulphide and the length of the exposure required to produce burns of equal intensity. The method used in working out this relationship was based upon that used in "gassing chambers."¹²

The principle was briefly as follows: Dry air was bubbled through dichlorethylsulphide at a known and constant rate, and mixed with a definite quantity of dry air also under constant flow for the purpose of dilution. A suitable glass exposing chamber was placed in the circuit near the bubbling tube,

using as little rubber tubing as possible for connections. (Rubber tubing absorbed the gas very readily.) The concentration could be determined by analysis of the escaping gas and air mixture from the open end of the exposing chamber, but could be accurately and more readily estimated by the loss-in-weight method, figuring the loss in weight of the bubbling tube after a certain period of time in relation to the known quantities of air employed. The skin of the forearm of the subject was shaved and sponged with alcohol and the desired exposures were made. Stress is again laid on the fact that readings were made after 24 and again after 48 hours, since the burns did not develop fully until that time. A faint disk of erythema was considered positive.

While curves drawn were apparently hyperbolic in form and consequently asymptotic, there appeared to be a critical level in concentration at approximately 0.002 to 0.005 mgm. of gas per liter at which no injurious effects were noted after prolonged exposures. From this it must be concluded that the amount of gas finding its way into the interior tissues after an exposure to the concentrations in question was no more than can be metabolized by the cells. This corresponds with previous observations regarding the threshold concentration of gas that can be disposed of without injury in prolonged respiratory tests.

It is essential to mention here that in determining the toxicity of dichloroethylsulphide on animals by inhalation a similar phenomenon was observed; data expressing the relation of time to concentration indicated a marked critical condition at this same mean concentration, 0.005 mgm. per liter. While the data for different species indicated differences in sensitivity, all indicated an ultimate threshold concentration within the limits of 0.01 and 0.001 mgm. per liter. It seems evident that this concentration represented a border line where the organism generally can metabolize the poison without serious effects.

It must be remembered that these experiments were originally carried out with a purely practical military objective: The determination of the relation between the concentration of gas and the time of exposure required to produce a burn under field conditions. It was fully realized that the loss from the skin by evaporation was considerable, and that exact scientific data regarding absorption of the gas by the skin and its penetration into the interior tissues could be secured only by covering the exposed area with some impervious substance immediately after the completion of treatment. Unfortunately, the suspension of experimental work on the cessation of hostilities prevented the carrying out of an elaborate series of experiments on these lines with varying concentrations of the compound. But from experiments with one concentration, to be reported later in this chapter, it has been demonstrated that the loss from the skin was extremely great, far exceeding the amount that penetrated the tissues, and for this reason it appears inadvisable to draw any far-reaching conclusions from the preceding curves.

The fact that a definite proportionality appears to exist between the increase in time at a given concentration and the increase in concentration at a given time required to produce equivalent effects in several individuals, suggests that the problem is one of satisfying the capacity of the skin to such an extent that the requisite amount of gas may penetrate to the interior tissues. The question as to whether this difference is due to the resistant man was made the subject of further experiments.

EFFECTS OF EVAPORATION

In considering any factor which is known to modify the final intensity of a mustard-gas burn, one must be careful to differentiate between those which modify absorption only and those which may have some effect upon the ultimate reaction which follows the introduction of the substance into those organized elements of the skin in which pathological effects are produced. Where the former may be brought about through simple physical means, the latter no doubt involve physiological relations of much more complex nature and are not dealt with in this chapter.

As previously explained, no attempt is made to specify what agencies are involved in the preliminary or final absorption of dichlorethylsulphide by the skin. The detailed localization of these agencies have not been found necessary to a clear conception of the general mechanism. Passing from the external absorbing agent previously indicated, the dichlorethylsulphide, in all probability, would pass through the deeper lying elements to the lipoid constituents of the cells of the adjacent tissues. If one were dealing with true absorption into the intermediary binder, the passage to the deeper tissues would probably be by diffusion from solid solution; on the other hand, its retention in this intermediary binder by absorption would make it highly probable that capillary and surface tension effects would direct it into the ducts, from which it would be taken up by absorption. On reaching the lipoids of the cell wall or cell contents proper, the mustard gas would slowly diffuse into the aqueous constituents of the cell, where hydrolysis of the compound would result and its toxic action would begin. Again attention must be called to the danger of attempting to localize the site or mechanism of this action from the evidence on hand. The nature of the poison may be such as to effect a fatal anesthesia of the vasomotor nerve supply, resulting in prolonged vasodilation and subsequent edema and vesication. On the other hand, there is abundant evidence from the work done by Lillie, Clowes, and Chambers on the penetration of marine eggs to indicate that the intracellular liberation of acid which would follow the hydrolysis of the dichlorethylsulphide would cause such profound changes in the protoplasmic equilibria of the cells concerned that their normal metabolism would be permanently upset and their permeability increased.⁵ From the evidence on hand, one is forced to believe that equal concentrations of the poison in this last phase (inside the cells of the tissues affected) would produce similar and nearly equal reactions in almost all men. Whereas the extreme difference in sensitivities of the skin represents an order of 1 to 600, the extreme difference in toxicity for any one species (dog), by inhalation or injection, is of a much smaller order, possibly 1 to 5. Exceptions to this equality of response to equal intracellular concentrations have been noted. One case has been reported where the subject (H. W. S.) developed an abnormal reaction suggesting an anaphylactic condition.

It has been suggested that after exposure of the skin to small amounts of mustard gas, evaporation from the surface has an important bearing upon subsequent absorption. To test this point, exposures to the vapors were made with the test-tube method previously described. Two exposures, just sufficient to cause a mild reaction, were made at the same time and under identical conditions. One was immediately covered with a shallow glass thimble of approximately the same diameter as the exposed area, fastened to the arm for three

hours or more with adhesive tape. The other was left uncovered, and served as a control. After 24 to 36 hours, when both burns had reached a maximal comparative development, the covered burn was seen to be much the worse. A series of experiments performed in this manner is tabulated in Table 36.

TABLE 36.—*Effects of evaporation after application of dichlorethylsulphide*

Subject	I Sensitivity	II Exposure	III Covered	IV Un- covered
C. R. M.	3 to 4 minutes	4 minutes	+++	++
F. W. W.	do.	3 minutes	+++	+
E. G. S.	2 to 3 minutes	do.	+++	+
J. W. W.	30 seconds	20 seconds	++	-
H. W. S.	10 seconds	10 seconds	+	+

Column I.—Subjects average minimum burning time to the standard test-tube, 20° C.

Column II.—Length of exposures made.

Columns III and IV.—Relative intensity of resulting burns: + + + severe erythema; + + mild; + faint; - negative. (Blistering burns were not made in any case.)

Sensitive men (i. e., men who gave a positive reaction to short exposures) generally showed less increase in reaction than did men who were relatively much more resistant. This suggested that the minimal burning time be determined when the exposed skin was subsequently covered for a prolonged period and compared with the minimal burning time when exposures were left uncovered.

From Table 37 it is apparent that the possible reduction in minimal burning time in a sensitive individual by covering the exposure was generally less than in a resistant individual.

TABLE 37.—*Effects of evaporation after application of dichlorethylsulphide*

Subject	When left uncovered, minimal burning time	Covered immediately for 10 hours	
		Length of exposure	Degree of burn
G. G. F.	3 minutes.	Seconds	
		1	Negative.
		5	Do.
		15	Positive.
		30	Do.
		60	Do.
C. R. M.	4 minutes.	30	Do.
F. W. W.	do.	15	Do.
		30	Do.
E. G. S.	2 to 3 minutes.	30	Do.
P. S. B.	20 seconds.	30	Do.
		1	Do.
		5	Do.
		10	Negative.
H. W. S.	10 seconds.	2	Do.
G. W. W.	30 seconds.	20	Positive.

This suggests that the skin of a resistant individual absorbed more of the dichlorethylsulphide than the skin of a sensitive one, because the only other apparent way in which covering could influence the final reaction would be by increasing the rate of passage of the sulphide from the outer layers of the skin to the inner layers through an increase in temperature and thus raise what would

naturally (uncovered) be a subreactive concentration to a reactive one. On such a basis it would seem obvious that a sensitive man would show relatively as great an increase in intensity as a resistant man. Against the argument that a sensitive man exhibits a close approach to the maximum reaction, and therefore can not be made to show a large increment over his normal reaction (uncovered), is the fact that individuals were known who blistered to a 5-second vapor exposure, and gave severe edema to less than 1 second, and in whose history there was nothing to indicate any anaphylactic or other abnormal reaction, beyond their great sensitivity. This problem will be considered later.

Another point of interest was the time an exposure must subsequently be covered to secure the maximum reaction on any one individual, thus finding the time during which the loss by evaporation would still produce an appreciable decrease in the final intensity of the burn. An experiment to determine this is given in Table 38. Exposures of border-line intensity were made and covered immediately, and were left covered for varying intervals.

TABLE 38.—*Effect of covering dichlorethylsulphide burns*

[Burns were covered immediately and left covered for varying intervals as indicated]

Subject	Sensitivity	Exposure	Time covered			
			15 minutes	30 minutes	45 minutes	60 minutes
C. R. M.	4 minutes	5 minutes	+	++	+++	+++
H. W. S.	10 seconds	do	++	++	++	---

In another experiment (Table 39) the approximate rates of evaporation and absorption were determined by covering mild exposures after varying intervals of time had elapsed during which the skin had been left open to the air.

TABLE 39.—*Effect of covering dichlorethylsulphide burns*

[Burns were covered after varying intervals had elapsed and left covered for six hours]

Subject	Sensitivity	Exposure	Left un- covered	Covered after exposure to air for —				
				0 minutes	15 minutes	30 minutes	45 minutes	60 minutes
H. E. I.	3 minutes	3 minutes	+	++++	+++	++	+	+
H. W. S.	20 seconds	15 seconds	—	+++	+	+	—	—

From these experiments it is evident that equilibrium in the skin was reached in about 45 minutes and that capping had less effect on a sensitive than on a resistant skin. This rate of attaining equilibrium must have had a direct bearing upon further absorption and, ultimately, upon sensitivity. Since the dichlorethylsulphide was at first absorbed by the surface of the skin or some superficial elements adjacent thereto, and could be lost from this medium by evaporation, the relation rate at which it passed from this intermediary binder to some other phase, in which it was firmly fixed, as against the rate at which it was lost by evaporation, would be the determining factor in the question of whether or not a slight exposure to the vapors would prove positive or negative.

Since the intensity of the burn produced by a given concentration bore a direct relation to the length of the exposure, and since in at least one case (H. W. S.) a reaction was produced within 10 minutes of exposure, it is probable that the velocity with which the substance passes from the surface to the deeper layers was such that the absorption of additional amounts was not interfered with. While the determination of the rate at which it passed from the surface inward was a problem of considerable complexity, the rate at which it was lost from the skin by evaporation was readily determined by a few simple experiments. By making a series of exposures of varying periods of time and covering certain of these exposures to prevent evaporation, it was possible to determine the time for which a short exposure must be covered to give a burn of equal intensity to an exposure of greater length which was left open to the air.

Two such experiments were made on the skin of the shoulders of two subjects (H. E. I and W. B. Mc.); the burns were covered immediately and left covered for the time given in the left-hand columns, Tables 40 and 41. An accurate representation of their relative severity after they had reached their maximum comparative development, as determined by the readings of three observers, is given. The system of nomenclature is simply an effort to give the relative severity of the burns in each set, and comparisons can not be made from one set to the other.

TABLE 40.—*Effect of covering exposures of varying lengths*

[H. E. I. Minimum burning time, 1 minute]

Time covered	Length of exposure				
	15 seconds	30 seconds	1 minute	2 minutes	3 minutes
0.....	—	—?	+	+++	+++
15 seconds.....	—	—?	+	+++	+++
30 seconds.....	—	—?	+	+++	+++
1 minute.....	—	+	+	+++	+++
2 minutes ¹	+?	+	+	+++	+++
4 minutes ¹	+	+	+	+++	+++
16 minutes.....	+?	+	+	+++	+++
32 minutes.....	+	+	+	+++	+++
64 minutes.....	+	+	+	+++	+++
128 minutes.....	+++	+++	+++	+++	+++

¹ In the exposures capped for 2 and 4 minutes it is probable that the thimbles were not tight. The skin used was on a curved surface of the shoulder and the resulting burns are undoubtedly low in intensity through this experimental error.

TABLE 41.—*Effect of covering exposures of varying lengths*

[W. B. Mc. Minimum burning time, 1 minute]

Time covered	Length of exposure				
	15 seconds	30 seconds	1 minute	2 minutes	4 minutes
0.....	—	—?	+	++	+++
30 seconds.....	—	—?	++	++	+++
2 minutes.....	—	—?	++	++	+++
8 minutes.....	+?	++	++	++	+++

Where Table 40 is a comparison of more intense burns, Table 41 is a comparison of threshold burns, i. e., where the exposure was just sufficient to produce a faint reaction.

Since a 15-second exposure could be increased by covering to the intensity of a 4-minute exposure, the amount lost by evaporation into the air must have been far in excess of that which passed into the deeper tissues. Experimental evidence was insufficient to determine the relative distribution between air and the skin. The practical importance of the fact of evaporation can not be overlooked, and its bearing on variations in cutaneous sensitivity will now be considered from another point of view.

TRANSFER FROM SKIN TO SKIN

An interesting phenomenon was observed when the untreated normal skin of one subject was impressed for 5 minutes upon an area of skin of another subject previously exposed to the vapors of dichlorethylsulphide. Under these circumstances, both donor and recipient might develop burns (due to the transportation of the poison from one skin to the other) the intensity of which would vary according to the circumstances and the respective sensitivities of the participants. The degree of transportation was most strikingly observed in the intensity of the burn on the donor's arm. If two similar exposures were made on the arm of a sensitive man, and one of these burns was treated, so to speak, by contact for 5 minutes with the skin of a resistant man, the treated burn would be markedly less severe than the control, in some cases being entirely prevented. If, however, the recipient was equally sensitive to or more sensitive than the donor, the burns on the latter exhibited far less difference. Both treatments could be effected at once, using two recipients, one more resistant, and one less resistant, than the donor. In such a case the burn brought in contact with the more resistant skin was the less severe.

A few experiments of this nature are given in Table 42. The subjects are divided for clarity into two classes, (R) resistant and (S) sensitive. It is evident that the "resistant skin" had reduced the burn with which it was in contact much more than had the "sensitive skin." One is forced to the conclusion that it had actually absorbed more of the gas.

TABLE 42.—*Transfer from skin to skin of dichlorethylsulphide burns*

Donor	Sensitivity	Recipients	Sensitivity	Burns exhibited by—	
				Donor	Recipient ¹
H. F. S.....	(S)	{ Treated by J. A.	(S)	++++	++
		{ Treated by C. R. M.	(R)	++	++
H. E. S.....	(R)	{ Treated by J. A.	(S)	++	++
		{ Treated by C. R. M.	(R)	++	+
J. W. W.....	(S)	{ Treated by H. W. S.	(S)	++	
		{ Treated by C. R. M.	(R)	+	

¹ It was found that if the burns on the recipients were capped, they would develop to approximately the same intensity, showing that the recipient's sensitivity conditions the final intensity of his burns, as might be expected.

This same experiment was carried out in the reverse order. Similar exposures were made on the arms of a sensitive and a resistant subject. Immediately after the exposure, a third subject received both burns by impressing them against his arm for 5 minutes. It was seen that a "sensitive skin" would take more of the poison from a "skin of equal sensitivity" than from a more resistant one.

Both experiments were, in fact, important evidence that the skin of a resistant individual exhibited a greater affinity or capacity for dichlorethylsulphide than that of a sensitive one. Whatever the arrangement of the experiment, the results indicate that there was an actual partition of the gas between the two skins, with an evident tendency to establish an equilibrium in which the largest portion of the gas would remain in that skin which possesses the greater capacity for it. The experiment confirms in a striking manner the observations noted above, and explains why equilibrium with the air is attained from a sensitive skin sooner than from a resistant one. This is directly contrary to the general belief that a resistant individual is more resistant to low concentrations of mustard gas than his fellows because his skin absorbs less. The assumption that his skin absorbs more makes it imperative that some explanation accounting for the paradox be made.

In order to determine the persistence of the gas on the surface of the skin after exposure, an experiment was made in which a series of 5-minute exposures were capped for 15 minutes, 30 minutes, 45 minutes, etc., and then impressed on the arm of a subject of about the same sensitivity for 5 minutes.

Since the recipient failed to develop a burn after contact with the burn on the donor, which had been capped for 60 minutes, it was apparent the gas had disappeared from the donor's arm in that period. This agreed well with the results obtained by capping in Table 39, in which a maximum absorption was indicated within that time.

TABLE 43.—*Sensitivity tests of dichlorethylsulphide burns*

Donor	Sensitivity	Recipient	Sensitivity	Intensity of the burn on recipient
1. C. R. M.	(R)	H. W. S.	(S)	1. ++
2. J. W. W.	(S)			2. +++
1. C. R. M.	(R)	E. K. M.	(S)	1. ++
2. J. W. W.	(S)			2. ++++

TABLE 44.—*Persistence of gas after dichlorethylsulphide burns*

	Time capped			
	15 minutes	30 minutes	45 minutes	60 minutes
Donor C. R. M. (R)	+	++	+++	+++
Recipient R. S. (R)	++	++	+	-

RELATION OF PHYSICAL PROPERTIES TO PENETRATION

It is generally recognized that substances possessed of the capacity of readily penetrating protoplasm are almost invariably soluble to a certain extent in water and are also "lipoid soluble," that is, soluble in fats and organic solvents such as benzene and xylene, and that the so-called partition coefficient between water and benzene or xylene is a factor of considerable importance in conditioning their power to penetrate living cells.

Some 25 compounds were investigated, so-called war gases, which were not only highly toxic, but which irritated the skin. The determination of their partition coefficients was a very difficult matter in most cases because

of their rapid hydrolysis in water (in such cases a strong acid is one of the decomposition products), but it was evident that they were all soluble in both lipid solvents and water to some extent. This fact, with the fact of their hydrolysis, suggested that the mechanism of their action could be correlated in a general way with that of dichlorethylsulphide. Further experimental work is necessary to establish this fact. This group of compounds in the category of war gases vary greatly in their degree of activity and in their specific toxic effects, and while no far-reaching generalization on this question will be attempted it is proposed at a subsequent stage in this chapter to discuss briefly certain cases in which toxic effects correlate in a measure with physico-chemical properties.

A series of experiments was performed with a number of organic bases in an attempt to determine their value as a means of counteracting the effects of mustard gas. It was found that with the exception of ammonia only those bases which were lipid-soluble irritated the skin, indicating penetration. On the other hand, too high a partition coefficient (too low solubility in water) appeared to diminish the irritating activity on the skin. (The following examples are representative of the groups tried: Ammonia, propylamine, ethylamine, amylamine, di-isoamylamine, bornylamine.) Whatever the interpretation of the details, it is apparent that lipid solubility is an important factor in the penetration of the intact skin.

A brief reference should be made to a phenomenon requiring further investigation. Field observers have noted that burns occur more frequently on moist than on dry portions of the body. This observation was confirmed in the laboratory and, furthermore, a film of water on the dry skin was found to facilitate the passage of mustard gas, showing that the effects observed in the field were not attributable simply to a possible higher permeability of freely perspiring areas, but was in some way attributable to the presence of water on the skin.

To determine whether this was attributable to surface effects caused by the presence of a film of fluid, a series of equal threshold burns were made over the dry skin and skin wet with various organic agents, care being taken in the case of each individual to select the exact time of exposure required to give a mild burn on the dry skin.

The fact that water is a very poor solvent for mustard gas and yet appears to facilitate the passage of the substance into the tissues as well as the other fluids which are good solvents for it, suggests the probability that capillarity rather than solution may play an important rôle in transporting mustard gas from the atmosphere to the point of entry into the skin, and lends some support to the view that mustard gas passes down the sweat glands by a process in which surface phenomena play an important part.

There is a striking correspondence between the above results in which a water film facilitates the passage of mustard gas into the tissues and the observation of Clowes, Perrott, and Gordon that the passage of mustard gas through clothing is facilitated by the presence of from 3 to 5 per cent of water.¹³

DISCUSSION

A variation in sensitivity of the skin of several hundred to one was observed in experiments with saturated vapor or paraffin oil solutions of dichlorethyl-

sulphide. In experiments with different concentrations and times of exposure, using different species of animals, the variation in the susceptibility of the individuals of a given species to the effects of inhalation were of a very much lower order of magnitude—probably not more than five to one. Furthermore, on intramuscular or intravenous injection in dogs variations of no great order of magnitude were observed. As pointed out in a previous portion of this chapter, it is evident that the differences in sensitivity observed were due to differences in the relative amounts observed compared with the amounts lost by evaporation. Hence one is justified in assuming that in individuals of the same species the amount of mustard gas required within the cell to produce pathological effects is roughly the same—that is, the threshold concentration for the cell varies very little in different men.

In discussing the mechanism of absorption of mustard gas by the skin it is proposed to consider the problem from the standpoint of a three-phase system in which the outer phase (A) represents the external atmosphere containing varying concentrations of mustard vapors; the middle phase (B) represents the outer layers of skin through which the mustard must pass in order to produce a toxic effect; and the inner phase (C) represents the inner layer of the skin, particularly the protoplasmic contents of those cells of the tissues which are directly affected by the poison.

For purposes of convenience A, B, and C in resistant individuals have been designated as A_r , B_r , and C_r , and in sensitive individuals as A_s , B_s , and C_s .

If, as has been indicated above, the velocity with which mustard gas must pass into those reactive cells which have been designated as C in order to produce a given pathological effect, is approximately constant in resistant and sensitive individuals—if the critical toxic threshold concentration in C_r is the same as in C_s —it necessarily follows that variations in concentration of gas or time of exposure in A required to produce equal effects in C_r and C_s must be attributable in great part to variation in the resistance offered by B_r and B_s to the passage of the gas.

The explanation for the difference in facility of passage through B_r and B_s may lie in one or more of the following causes: (1) Variation in facility of absorption of mustard gas on interface between A and B. (2) Variation in the facility with which absorbed mustard gas passes along gland surfaces by capillarity or into and through the epidermis by a process of diffusion of the absorbed or dissolved gas. (3) Variation in the thickness of B_r and B_s or the actual distance to be traversed from A to C. (4) Variation in the amount of gas required to saturate constituents of the skin which may be capable of adsorbing or dissolving large quantities of the gas (for example, lipoids, pigment granules, etc., in negro and white skin). (5) Variation in the facility of passage of gas from B into C particularly from the lipoid nonaqueous phase into the aqueous phase of the protoplasm of those reactive cells in which the pathological effects are produced.

It is difficult to determine the relative importance of the rôle played by each of these factors, but variation in the resistance of B may be conveniently represented pictorially either by varying its thickness, making B_r thicker than B_s , or by varying the angle of the average gradient of mustard-gas concentration through B required to deliver a given amount of mustard gas in C; in which case that of B_r would be steeper than B_s .

It will be seen that in either case, a critical concentration of mustard gas would be delivered into C_s with greater facility than into C_r ; thus a shorter exposure or a lower initial concentration would be required to effect the passage into C_s of a reactive quantity of the poison.

Whatever mode of expression be adopted, the effect of evaporation after the exposure is evident. The concentration at the interface AB would be higher than at the interface BC, but it would rapidly decrease as a result of loss into the air.

The delivery of the necessary critical concentration of gas into C for a sufficient period of time to cause pathological changes would obviously depend upon the thickness of B, upon the angle of gradient of resistance to passage through B, and upon the facility with which the concentration falls off at the interface AB as a result of evaporation. It appears desirable to utilize the available experimental data in an attempt to determine more specifically the relative importance of the individual factors enumerated above, viz, surface adsorption, resistance to passage of the gas, thickness of the skin, saturation capacity and threshold concentration required to produce toxic effects in C.

This last factor—i. e., threshold concentration in C—must be very low because (1) concentrations in the range of 0.002 to 0.005 mg. per liter represent not only critical points in the curves determined on the skin but (2) also correspond very closely with the threshold concentrations observed in respiratory experiments, and (3) the enormous proportion of gas lost from the skin after exposure, as shown by capping experiments, indicates that the amount which is absorbed is very small. The extremely small amounts to which some individuals give a reaction is further evidence for this fact. This low threshold concentration in C leaves adsorption on the skin surface or one or more of the factors involved in the passage through B, as primarily responsible for the buffer effect exerted by the skin.

In the case of liquid burns or severe vapor burns the difference in the protective mechanism of resistant and sensitive skins appears to be reduced to a minimum; all the factors involved are probably saturated, whatever their capacity.

The observation that the difference between B_r and B_s is more and more accentuated with reduction in time of exposure or concentration points to surface adsorption as an important factor; reasoning in this direction is supported by the following facts:

(1) Ten minutes after exposure of the skin to liquid mustard gas so large a proportion of the mustard gas may be removed by repeated washings with kerosene as to reduce the amount passing into the tissues below the critical level required to produce a blistering burn. (2) Washing with soap and water produces a corresponding effect, but to a much less degree. (3) The presence of mustard gas on the skin surface may be demonstrated half an hour after exposure by transmitting a burn to another individual. (4) Since a 15-second exposure may be raised by capping for an hour to the magnitude of a 3-minute exposure, the loss from the skin to the atmosphere must be far in excess of the amount passing into the interior. This suggests that the maximum concentration of mustard is on or near the surface. (5) The curves covering these capping reactions support the theory that surface adsorption is the factor of primary importance. (6) The fact that the skin may be left open to the atmosphere

for a prolonged period, in some cases as much as 30 minutes after exposure, and the intensity of the burn may still be raised by capping, indicates that loss of gas from the surface is still taking place. (7) The affinity of the skin of the resistant individual for mustard gas is far in excess of that of a sensitive one. The fact that B_r withdraws gas from B_s shows that B_r adsorbs gas more strongly than B_s and that the gas is still on or near the surface. (8) If exposures on resistant and sensitive skins have been so adjusted as to give equal burns if subsequently left uncovered, capping the exposures gives a worse burn in the resistant than in the sensitive case. This result corresponds with the fact that gas may be withdrawn by a resistant skin from a resistant skin longer than from a sensitive skin.

From the above considerations it seems probable that difference in the adsorptive capacity of the skin surface is the most important limiting factor in determining the degree of exposure in A necessary to effect the delivery of a toxic concentration in C.

In considering the relative importance of factors other than the surface adsorption on B and threshold concentration in C, it is obvious that the greater resistance of the negro's skin as compared with the white's skin may reasonably be attributed, in part at least, to differences in actual thickness of the skin, to fats and lipoids which appear to be more plentiful and to pigments which are known to be more plentiful in the negro skin than in white.

The very short minimum time within which the first reactions become visible in certain sensitive individuals would seem to indicate that the first traces passed through the skin fairly rapidly.

The experiments with water films seem to support the view that mustard gas passes into the sweat glands from which it is adsorbed after passing by capillarity to areas adjacent to the cells of the underlying tissues in which pathological effects are produced.

The capping experiments support this view. The passage of mustard gas into the sweat glands would obviously be facilitated by maintaining the vapor pressure.

These experiments should be considered in the light of certain observations concerning the absorption of dichlorethylsulphide in other parts of the body.

Even though mustard gas is very rapidly hydrolyzed at body temperature, inhalation of high concentrations of the vapor, intravenous injection of large quantities of the saturated aqueous solution, and application of the oil to the skin, cause not only local lesions but also marked and characteristic systemic effects.

It is obvious, therefore, that after its introduction into the blood stream a portion at least of the unhydrolyzed material must be taken up by lipoidal constituents and thus protected from immediate hydrolysis. After intradermal, subcutaneous, intraperitoneal or intramuscular injections of this substance the severe necrotic lesions which might be expected from its action are not observed. The pathological changes consist largely in the development of intense edema at the site of injection, with the characteristic effects on the gut and adrenals. It is possible that, when it is thus injected directly into the deeper tissues which are well supplied with blood, and which lack the nonaqueous binder of the skin, it is rapidly absorbed without doing much local damage. Moreover, the bountiful blood supply would go far to counteract the intracellular liberation of acid, and would thus circumvent its local toxic action. This suggestion is supported by the pathological changes observed in the respiratory tract in animals

gassed with mustard gas. Though congestion and necrotic sloughing appear in the upper tract, the lower tract is practically undamaged until very high concentrations are used, when some edema may appear. Since the lower respiratory tract is primarily an absorbing tissue, it is in very close association with the blood stream. The absorbed poison might be rapidly removed, and such hydrolysis as would inevitably occur might be counteracted by neutralization in the buffer system of the blood.

In considering the toxic action of a series of war gases it is observed that there is marked contrast in the pathological effects exerted upon the upper and lower respiratory tract and upon the skin.

There appears to be a certain relation between the areas inhibiting maximum pathological changes and certain physical and chemical properties of the gas, for example, vapor pressure, lipoid-water distribution coefficient and rate of hydrolysis in water.

Phosgene and superpalite, which have a very high vapor pressure and which hydrolyze very rapidly on contact with water, exert a very destructive effect on the lower respiratory tract, but do not markedly affect the upper tract or irritate the skin.

It is obvious that under a given condition of vapor pressure, lipoid solubility and other factors, a given amount of gas finds its way into the cell in a given time and if the rate of transportation through the cell is very rapid, the question as to whether or not a toxic concentration of acid will be produced within the cell depends upon the rate of hydrolysis, or the relation between transportation velocity and rate of hydrolysis.

A low lipoid-water partition coefficient should facilitate the decomposition of gas within the cell by raising the concentration in the water phase and by diminishing the proportion removed by the lipoid constituents of the blood.

The failure of such volatile substances as phosgene and superpalite to exert any effect on the skin is readily explained in the light of experiments with mustard gas, the loss of which from the skin to the air has been demonstrated to be very great in spite of its relatively low vapor pressure.

Substances like mustard gas, with a low vapor pressure and which hydrolyze comparatively slowly, would, after their absorption by the lower respiratory tract, have an opportunity to pass into the lipoidal phases of the blood before hydrolysis reached such dimensions within the cell as to cause pathological effects.

But in the cells of the upper bronchi and the skin, where transportation is comparatively insignificant, an accumulation would result, and ultimately sufficient acid would be liberated to produce toxic effects.

Phenyldichlorarsine and ethyldichlorarsine, with a low vapor pressure (resembling mustard gas somewhat in their physical properties) but having a high rate of hydrolysis, attack the skin and upper respiratory tract just as mustard gas does, and cause profuse edema in the lower respiratory tract just as do phosgene and superpalite.

Unfortunately, these investigations were incomplete when the suspension of hostilities brought an end to experimental work.

Consequently, though a large amount of additional data is available suggesting a relation between the physicochemical and pharmacological properties of substances which played a rôle in chemical warfare, it does not appear advisable to attempt further generalization at the present stage of our knowledge.

SUMMARY

The experimental data indicate—

1. That mustard gas is first absorbed by some element on or immediately adjacent to the skin surface.
2. That while a portion of the mustard gas passes rapidly inward to a point from which it can not subsequently be removed the greater portion remains on or near the surface for a considerable period, a proof of which is that it may be removed even after 10 or 15 minutes by persistent washing with organic solvents.
3. That the amount of mustard gas passing into the atmosphere from an exposed surface far exceeds the amount passing into the inner strata of the skin. This loss is very great at first and is still demonstrable after 45 minutes.
4. That the time of exposure necessary to produce a positive reaction bears a definite relation to concentration and varies for different individuals.
5. That a resistant skin absorbs far more gas than a sensitive skin, and gas may be withdrawn from the latter by the former. That difference in sensitivity of different skins is due principally to difference in saturation absorptive capacity.
6. That the intracellular threshold concentration of gas required to produce pathological changes in the skin is approximately the same in resistant and sensitive individuals.

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CHAPTER XIII

THE PHYSIOLOGICAL ACTION OF MISCELLANEOUS GASES

In the following pages is given a brief indication of the physiological action of a variety of gases possessed of possibilities as agents in chemical warfare. More detailed account of the physiological effects of the gases enumerated is not possible at this time, since extensive investigation in this direction has not been carried through.

CYANOGEN DERIVATIVES

CYANOGEN¹ (CN)₂

In its action cyanogen belongs to the group of paralyzants, and in general the symptoms produced are similar to those for hydrocyanic acid. The minimum effective concentration in animals is about 1 to 3,000, or 0.75 mgm. per liter of air for an exposure of 30 minutes. The minimum lethal concentration is 1 to 2,000, or 0.928 mgm. per liter. The gas is rather less poisonous than hydrocyanic acid.

SYMPTOMS IN ANIMALS

The symptoms produced after experimental gassing by cyanogen were rapid respiration, followed later by spasm and unconsciousness, during which the respiration became extremely slow and spasmodic in character. There were differences in the symptoms elicited by cyanogen and by hydrocyanic acid. With cyanogen there was an early stage of sneezing, lacrymation, and salivation arising from local irritation. The symptoms set in much later than was true for hydrocyanic acid. Spasms from hydrocyanic acid began within a few minutes after contact with the poison; that is, while the vapor was present in full strength. The cyanogen spasm at low concentration began only about 20 minutes after the administration, the animal remaining practically normal during the latent period, except for the symptoms of local irritation. The whole train of events suggested that possibly the cyanogen was rather slowly transformed to hydrocyanic acid in the tissues and that the intoxication was due to the cyanide rather than to the cyanogen. Animals quickly recovered (except for some soreness of the eyes) when they were withdrawn from the poisonous atmosphere as soon as spasms began and some warning was given by the extraordinarily quick, panting respiration.

HYDROCYANIC ACID² (HCN)

In animals (mice and dogs) this substance acted by a short preliminary stimulation, followed by paralysis of the nervous system. Death was caused by failure of the respiratory functions due to a paralysis of the respiratory center. It was not a lung irritant or lacrymator, but acted only after absorption into the circulation.

SYMPTOMS

The first symptoms were muscular weakness and often vomiting. This was followed by partial loss of coordination and dyspnea, which increased in violence until convulsions occurred. At this stage the pupils were dilated,

the limbs were rigid, and the eye reflex was absent. The convulsions occurred after this and were followed each time by a period of calm, in which respiration often ceased for nearly a minute. The respiration become more and more irregular until it finally ceased altogether, following which the heart beat stopped. At high concentration (0.5 mgm. per liter) convulsions set in almost immediately, death following in four or five minutes. At very low concentrations, the symptoms were slower in onset and much less severe. There were no delayed symptoms after exposure to this gas and recovery always occurred if the animal survived for a period of two hours.

The following were the relative concentrations necessary to kill the species enumerated.

	Dog	Cat	Rat	Goat	Rabbit	Monkey
Concentration G. M.	0.33	0.5	0.9	1.0	0.6	1.0
Concentration percentage of dose fatal to dog	100	150	270	300	180	300
Toxicity HCN to different species (reciprocals of above) ..	100	67	37	33	55	33

With hydrocyanic acid, species seemed to be a much more correct guide than size, while both differed from man; yet experience has shown that a man can exist without serious injury to himself in 1 to 2,000 HCN for a minute and one-half, this being lethal to dogs.

CYANOGEN CHLORIDE³ (CNCl)

A considerable variation in susceptibility to the toxic effects of cyanogen chloride was evident when different species of animals were employed (Table 45). The guinea pig, mouse, rat, dog, and the canary were studied. The following conclusions may be drawn. Guinea pigs appeared to be the most resistant and dogs the most sensitive of the animals studied. For each animal there appeared to be a different concentration below which death did not take place, regardless of the length of exposure. This was probably the concentration that may be destroyed or detoxicated by the particular species. Animals died very shortly after exposure to this gas or ultimately completely recovered. There appeared to be no delayed action. In field trials with this gas, guinea pigs should be among the animals employed in offensive experiments and dogs among those for defensive investigation. A few experiments with the monkey indicated that this animal is very little more resistant than the dog. Canaries were much more susceptible than any of the animals studied and may prove useful as test objects for this gas in manufacturing operations.

TABLE 45.—*Animals gassed with cyanogen chloride*
A. TIME REQUIRED TO ULTIMATELY KILL VARIOUS SPECIES

[Milligrams per liter; time in minutes]

	Concentration						
	0.85	0.75	0.65	0.55	0.45	0.35	0.25
Guinea pig.	14	18	25	41	60	87	116
Rabbit.	7½	14	22	33	45	60	87
Rat.	8½	11	13	17	22	27	37
Mouse.	7½	8½	11	16	23	34	60
Dog.	3½	5	6	8½	11	12	20
Canary.			1				

TABLE 45.—*Animals gassed with cyanogen chloride*—Continued

B. CONCENTRATIONS (MILLIGRAMS PER LITER) REQUIRED TO KILL DIFFERENT SPECIES

	Length of exposure				
	7½ minutes	15 minutes	30 minutes	60 minutes	120 minutes
Guinea pig.....	1.30	0.81	0.60	0.51	0.51
Rabbit.....	.85	.74	.58	.45	.45
Rat.....	.89	.60	.30	.18	.14
Mouse.....	.77	.58	.38	.25	.17
Dog.....	.68	.29	.20	.14	.14

SYMPTOMS

Dogs.—The symptoms during exposure were very similar to those of hydrocyanic acid poisoning, with the addition of irritation symptoms of the eyes, nose, and respiratory tract. The animal immediately exhibited irritation of the eyes and nose, then lacrymation and salivation. Retching and vomiting were observed in most instances, except where the concentrations were very high and convulsions set in very soon. The respiration was generally at first rapid, then slow and labored. Convulsions, prostration, unconsciousness, and death ensued if the concentration was lethal for the period of exposure. Death might occur during the exposure or within 5 or 10 minutes after removal from the atmosphere of the gas. There were no delayed deaths. If an animal lived for from 15 to 20 minutes after removal, he survived. Depression, slightly difficult respiration, discharge from the eyes and nose, and clouded cornea sometimes existed for a few days.

Mice.—The symptoms during exposure were immediate excitement, irritation of eyes and nose, dyspnea, depression and convulsions, prostration, gasping, and death, provided the concentration was lethal for the period of exposure.

Rats.—The symptoms were very similar to those shown by dogs exposed to this gas.

Rabbits.—During exposure the symptoms were in order of their occurrence as follows: Immediate irritation of eyes and nose; excitement for a few minutes; salivation; then depression, the animal keeping its head thrown back and breathing in deep gasps, with long intervals between gasps. If the concentration was lethal for the period of exposure the animals later recovered, being very much excited for a few moments, and then passed into convulsions and lay prostrate and gasping. Death occurred in from a few minutes to half an hour. If the animal survived, it was likely to be apparently quite normal the day following exposure.

Guinea pigs.—Animals exposed to toxic concentrations exhibited the following symptoms: Irritation of eyes and respiratory tract; lacrymation, salivation, excitement, paralysis, prostration, convulsions, and gasping. Animals invariably recovered if they survived exposure to the gas and lived a few hours afterwards. Out of a total of 61 animals exposed, no delayed deaths occurred

CYANOGEN BROMIDE* (CNBr)

Of the species of animals exposed to the toxic action of the true vapor of this substance the dog and rat were of about equal susceptibility and were the most resistant; the mouse was the most susceptible; the guinea pig and rabbit were of about an equal degree of susceptibility and occupied an intermediate position.

The pharmacological action of this substance was apparently twofold: (1) There was an action similar to that of hydrocyanic acid or cyanogen chloride on the control nervous system, causing death by paralysis of the respiratory center, and (2) an irritant action in the lungs, causing delayed death, probably by lung edema. An animal which survived the first action might later die from the second. The relative intensity of these two actions seemed to differ in different species.

The results obtained in regard to the species and time variation with this substance are summarized in Table 46.

TABLE 46.—*Animals gassed with cyanogen bromide*

A. TIME REQUIRED TO KILL VARIOUS SPECIES

[Milligrams per liter; time in minutes]

	Concentration			
	1.00	0.85	0.55	0.25
Rat.....	8	10	17	110
Dog.....	7½	9	17	135
Guinea pig.....	5½	8	18	48
Rabbit.....			13	35
Mouse.....				15

B. CONCENTRATION (MILLIGRAMS PER LITER) REQUIRED TO KILL DIFFERENT SPECIES

	Length of exposure				
	7½ minutes	15 minutes	30 minutes	60 minutes	120 minutes
	Concentration of gas				
Rat.....	1.10	0.60	0.38	0.31	0.23
Dog.....	1.00	.60	.39	.30	.26
Guinea pig.....	.82	.61	.38	.22	.19
Rabbit.....	.72	.49	.30	.15	.10
Mouse.....	.40	.25	.18	.17	.15

SYMPTOMS

Inasmuch as the symptoms elicited were more or less similar in the various species of animals studied, only those for the dog need be detailed. During the exposure there was immediate irritation of the eyes and respiratory tract, then lacrymation and salivation. At the higher concentrations the animal might become wildly excited, have convulsions, and become paralyzed within a few minutes. Death could occur during the exposure, minutes afterward, or might be delayed for several hours or days. Retching or vomiting occurred usually even with the lower concentrations. Clouding of the cornea sometimes occurred during the exposure. With concentrations as low as 0.20 mgm. per liter death with convulsions might occur during the exposure provided it was sufficiently prolonged. Even after having had severe convulsions and paralysis during exposure, dogs could recover from the immediate effects and either die later from lung damage or survive. Animals which survived the immediate action usually had severe respiratory symptoms. Marked depression, sore eyes, with swelling of the cornea, and nasal discharge generally occurred. If the animal survived the symptoms might persist for from 3 to 10 days. Delayed deaths from the lung irritant effect of the gas usually occurred within 48 hours, although some animals died 5 days later.

ARSENIC DERIVATIVES

ARSINE⁵ (AsH_3)

Arsine produced no striking symptoms in animals exposed to it. It is true that there might be slight shivering and some evidences of depression toward the end of the period of exposure. In one or two instances there was vomiting and slowing of respiration. The animals (dogs) exposed to both high and low concentrations of arsine were usually very depressed for a number of days, voiding bloody urine and black stools. They usually refused food and seemed to have little or no appetite for a time and then ate very sparingly. These animals showed symptoms for a considerable period of time. Some days they seemed apparently normal and then would show depression, alternating this way for weeks. The toxic concentration might be placed at 0.33 mgm. per liter. Arsine was fatal in the ratio of 1 to 2,000 inhaled for 20 minutes. On the other hand, exposure for 20 minutes to an atmosphere of 1 to 5,000 was not fatal, and in concentration of 1 to 20,000 no harm seemed to result during the above-mentioned period of exposure.

Experimental observation on animals, as well as reports of human cases, point to the conclusion that the toxicity of arsine was due in large measure to hemolysis. The striking clinical symptoms of this action were hemoglobinuria, hemoglobinemia, icterus, and rapidly developing anemia. Upon the entrance into the blood of arsine it is taken up by the red corpuscles, forming a compound which imparts a brown color to the blood. In the presence of the oxygen in the corpuscles, the arsenic hemoglobin compound is gradually converted into arsenic oxide, and during this process of oxidation hemolysis takes place. In the kidney, hemoglobin thus liberated is partially converted into methemoglobin, which appears in the urine, together with oxyhemoglobin.

ARSENIC TRICHLORIDE⁶ (AsCl_3)

In high concentration mice were very much excited and showed respiratory difficulty. The eyes were inflamed and there was a nasal and lacrymal discharge. Finally, convulsiform movements were followed by what appeared to be a marked depression. In lower concentrations the symptoms were less marked and were those of local irritation—closing the eyes, rubbing the nose, and nasal and lacrymal discharge. The toxic concentration was 2.5 mgm. per liter of air. The effects observed were those of a combination of arsenical and hydrochloric acid poisoning.

ARSENIC TRIBROMIDE⁷ (AsBr_3)

Mice exposed for a period of 10 minutes to vapors of arsenious bromide showed very marked nasal irritation, dyspnea, and later occasional gasping. The toxic concentration of this substance for mice on 10 minutes' exposure may be placed at 2.0 mgm. per liter, 100 per cent of the mice dying in 48 hours.

ARSENIC TRIFLUORIDE⁸ (AsF_3)

The toxic concentration of arsenic trifluoride for mice was reported as 0.7 mgm. per liter of air. The symptoms were as follows: Nasal irritation is shown by vigorous rubbing of the nose. The eyes soon became moist and were then closed tightly. Dyspnea and gasping soon occurred. The extremities were very cyanotic at the end of exposure. The skin was ashen in color at death which usually occurred within 24 hours.

For dogs the toxic concentration was 0.73 mgm. per liter of air. The symptoms follow:

SYMPTOMS DURING EXPOSURE

At all concentrations from 0.13 to 0.81 mgm. per liter there was severe irritation of the eyes and mucous membrane of the nose and throat; lacrymation, salivation, and nasal secretion were in most instances profuse. Several of the animals sneezed, retched, and vomited.

SUBSEQUENT SYMPTOMS

Dogs exposed to a concentration of 0.53 mgm. per liter or above were very depressed after exposure. Within 24 hours they had developed sore eyes, a wheeze or cough, and were very much depressed. There was also dulling of the cornea after the second day. In the cases of dogs surviving, this condition persisted for 10 or 12 days without very marked improvement. The deaths occurred in from 2 to 4 days. Dogs exposed to lower concentrations showed only slight depression but this condition persisted for a number of days without marked improvement.

USE AS A SKIN IRRITANT

Arsenic trifluoride was one of the important skin irritants. Its effects were felt almost immediately upon application. Dilution with alcohol (1:25 to 1:100) showed some irritation but, aside from a slight temporary discoloration of the skin, there was no reaction. A dilution of 1 to 500 in alcohol showed no symptoms in seven days.

Immediately upon application of the undiluted substance, the skin was discolored, the rabbit struggled violently, as though in considerable pain, and the respiratory rate was considerably increased. Both animals tested died within 24 hours.

DICHLORMETHYLARSINE⁹ (CH_3AsCl_2)

The toxicity of dichloromethylarsine approached that of phosgene. The symptoms included an initial period of excitement, which was soon followed by an interval of depression. For about 5 minutes of exposure there were alternate periods of activity and depression. Finally the mice became greatly depressed. Intense irritation of the nose and eyes was evident. Hyperemia of the nose and eyelids were marked, and both a nasal and lacrymal discharge occurred. Respiration was deep, slow, and irregular. Death usually occurred within 24 hours.

SKIN IRRITANT PROPERTIES

This poison was less irritating than phenyldichlorarsine, probably because of its higher volatility, and it was more irritating as a gas. The vapors were as irritating as mustard gas; the liquid seemed somewhat more irritating. The vapor caused immediate hyperemia of a light pink color, with very marked swelling. In 24 hours a capillary hemorrhage appeared and the swelling had mostly receded. After four days the local area was as intense as one treated with phenyldichlorarsine, but there was no spreading.

CACODYL CHLORIDE (CHLORODIMETHYLARSINE)¹⁰ $((\text{CH}_3)_2\text{AsCl})$

This poison is less toxic than arsine. A cat exposed to a concentration of 1 to 1,000 cacodyl chloride for one hour showed progressively increasing dyspnea, became comatose 2 hours after removal, and died about 10 hours later. A cat exposed to a concentration of 1 to 10,000 cacodyl chloride for a period of 1 hour developed marked dyspnea; food was refused on the following day, and the animal gradually became apathetic and died on the fourth day. A cat exposed to the gas in a concentration of 1 to 50,000 for a period of 1 hour showed no effects except the secretion of thick saliva. It remained well after removal from contact with the poison.

CACODYL CYANIDE¹¹ $((\text{CH}_3)_2\text{AsCN})$

This substance had an irritant action both on the eyes and on the respiratory passages. The former action, however, was less powerful than that of various other lacrymators tested. The physiological action and effects of cacodyl cyanide varied somewhat from those of substances previously investigated. The prominent features were the following: There was no appreciable lacrymation at concentrations of less than 1 in 1,000,000. Lacrymation was very pronounced with three out of four subjects (men) who reached a concentration of 1 in 125,000. Nasal irritation was definite, inducing in the higher concentrations an attack of sneezing. The odor and taste had a distinct tendency to produce nausea. In three cases a definite sensation of giddiness and a feeling of compression in the head was experienced.

ETHYL ARSINE¹² $(\text{C}_2\text{H}_5\text{AsH}_2)$

For mice the toxic concentration of this gas was 6.5 mgm. per liter of air. At concentrations of 47 and 69 mgm. per liter there was marked nasal irritation, continued gasping, convulsions, and death in a few minutes. After death there was a marked flexor rigidity. At concentrations of 10 and 6.5 mgm. per liter there was marked nasal and lacrymal irritation. There was a brief period of increased activity which was soon followed by deep depression. The respiration was deep and irregular at first, but soon became rapid and shallow. Near the end of the period of exposure, the mice became weak, uncertain in movements, trembled convulsively, and finally became prostrate. Death occurred within 30 minutes after exposure and was preceded by a brief convulsion. At a concentration of 1.5 mgm. per liter both nasal and lacrymal irritation were shown. A brief period of increased activity was succeeded by deep depression. Respiration was slow, shallow, and irregular, with occasional gasping.

DICHLORPHENYLARSINE¹³ $(\text{C}_6\text{H}_5\text{AsCl}_2)$

EXPERIMENTS WITH MICE

During the period of exposure there was very marked irritation of the nose and eyes, with lacrymation, and hyperemia of the nose and eyelids occurred almost immediately. Dyspnea, with occasional gasping, was shown in a few minutes, and gasping became convulsive and almost continual near the end of the exposure. One of the two mice exposed to a concentration of 0.18 mgm. per liter died within 48 hours, with no external evidences of irritation. The other mouse, on the seventh day, developed a marked swelling of the head.

On the tenth day its head and back were covered with dry ulcers. The skin seemed to have cracked and curled up leaving a dry ulcer. The hair had fallen off one side of its head, while its ears were dry, shriveled, and stiff. The eyes were closed by a yellow secretion. On the fourteenth day the swelling of the head had decreased and the right ear had dropped off close to the base. On the sixteenth day the swelling had entirely disappeared, the eyes were clearing of the secretion, and the hair had dropped off both sides of the head and in spots on the back. The ulcers on its head and back seemed to be healing. On the seventeenth day the left ear had dropped off, the eyes were partially open, and the discharge from them was watery instead of thick and yellow as before. On the nineteenth day more hair had dropped off the head and back. On the twenty-first day one eye was entirely open, while the other was partially closed. Both seemed weak and the watery discharge still continued. The ulcers had entirely healed.

Of the two mice exposed to a concentration of 0.13 mgm. per liter, one died in 22 hours. The other at the end of 10 days had developed swelling of the hind legs, feet, and head. Its ears were shriveled and hard. It died on the seventeenth day. The skin was cyanotic, ears shriveled, hind feet swollen and ulcerated. The mice exposed to a concentration of 0.08 mgm. per liter at the end of 10 days were both alive. The ears were dry and shriveled, the head and back were ulcerated, and the hair was coming off the head and back.

EXPERIMENTS WITH DOGS

At all concentrations there was severe irritation of the eyes and mucous membrane of the respiratory passages. Dogs exposed to concentrations of 0.06 mgm. per liter and above showed excitement, severe irritation of the eyes, lachrymation, salivation, retching, vomiting, and sneezing. At a concentration of 0.02 mgm. per liter there was still irritation of the eyes and nose, but one dog exposed to 0.01 mgm. per liter showed no symptoms during exposure.

Within 24 hours after exposure all the dogs exposed to concentrations of 0.02 mgm. per liter and above had sore eyes, cough, rattle or wheeze, and were generally very depressed. This condition persisted for 5 or 10 days, or longer in cases where the animals had been subjected to sublethal concentrations. Four deaths occurred in from 18 hours to 3 days. One was delayed after exposure. Two dogs exposed to a concentration of 0.25 mgm. per liter died within 3 days. Of 4 dogs exposed to concentrations of 0.14 and 0.21 mgm. per liter 3 survived. The toxic concentration may be placed at 0.26 mgm. per liter of air.

SKIN IRRITANT PROPERTY

Phenyldichlorarsine produced marked swelling in 15 minutes, which increased throughout a period of from 6 to 8 hours. It was accompanied by a quick hyperemia and in from 3 to 6 hours by very extensive hemorrhages. The exposed area became white and hard, having the appearance of entirely dead skin. The hardening of the skin and the translucent white color gradually replaced the capillary hemorrhage until only a small hyperemic area was left encircling the burn. It appeared from its immediate action that phenyldichlorarsine was a much more severe irritant than mustard gas. A burn up to 4 days old would be judged three to four times as extensive as a mustard-gas burn of the same age and equally severe.

DIPHENYLCHLORARSINE¹⁴ $((C_6H_5)_2AsCl)$

This gas was a lacrymator and a respiratory irritant. Very minute amounts caused sneezing. Large amounts caused painful irritation of the respiratory tract. The gas produced headache, giddiness, and depression, which soon wore off. There were no after effects and no visible influence on the skin. One part in 500,000,000 was intolerable for continuous respiration.

EFFECT ON MAN

One part of the gas in 100,000,000 (0.00012 mgm. per liter) was just detectable. One part in 50,000,000 (0.00024 mgm. per liter) caused nasal irritation after two minutes. One part in 20,000,000 (0.0006 mgm. per liter) induced marked nasal irritation without sneezing. One part in 1,000,000 (0.0012 mgm. per liter) became intolerable with or without the eyes protected. It also produced severe irritation of the respiratory tract.

INFLUENCE ON MICE

The gas in small concentrations was not very toxic, as mice continued to live for nine days in an atmosphere of 1 to 2 parts per million.

ACTION ON DOGS

At a concentration of 0.02 mgm. per liter and above the animals showed immediate excitement, and severe irritation of the eyes and mucous membrane of the nose and throat. Salivation and lacrymation were profuse and there was increased nasal secretion. Dogs exposed to concentrations below 0.2 mgm. per liter showed few or no symptoms. Three dogs exposed to a concentration of 0.06 mgm. per liter or higher were very depressed, had sore eyes, increased nasal secretion and developed a bad cough and rattle in the throat. One animal exposed to a concentration of 0.1 mgm. per liter died in six days. Another dog exposed to a concentration of 0.09 mgm. per liter was in very bad condition at the end of 10 days and did not seem likely to recover. The animal exposed to a concentration of 0.06 mgm. per liter had apparently recovered at the end of eight days. Below this concentration the dogs with a single exception recovered.

SUSCEPTIBILITY OF DIFFERENT SPECIES

Dogs and monkeys are killed by approximately the same doses. Expressed as fatal concentrations relative to that for the dog, the following results were obtained for different species:

	Dog	Cat	Rat	Goat	Rab- bit	Mon- key	Guinea pig
Fatal concentration, percentage of dose fatal to dog.....	100	220	220	220	400	135	33
Toxicity of $As(C_6H_5)_2Cl$, different species, reciprocal of above..	100	45	45	45	25	75	300

The following gives the comparison with phosgene and chloropicrin at the concentration which was fully tested; i. e., 1 in 200,000 for 30 minutes exposure: Chloropicrin killed goats, monkeys, and guinea pigs; did not kill dogs, cats, rabbits, or rats. Phosgene killed cats, rabbits, rats, monkeys, and guinea pigs; did not kill goats or dogs. Diphenylchlorarsine killed goats, dogs, cats, monkeys, and guinea pigs; did not kill rabbits or rats.

SKIN IRRITANT PROPERTIES

There was no swelling or hyperemia in 45 minutes. In 90 minutes the skin presented a white, blistered appearance. After 2 hours some hyperemia and swelling appeared, and the former became very distinct in 6 hours, but with no spreading through the unexposed skin. In 24 hours the area of exposure was swollen equally with a mustard-gas control, and was deeply hyperemic, but there was not the lateral swelling presented by the mustard-gas control.

Diphenylchlorarsine was a strong irritant, but doubtfully as strong as mustard gas and certainly far less irritant than phenyldichlorarsine. The vapor yielded negative results.

Using a saturated solution in carbon tetrachloride, application to the flexor surface of the forearm for 10 to 20 minutes gave no abnormal sensation. At the end of the application the skin was reddened and a papular erythema developed. A warm solution applied for 10 minutes gave a more marked erythema, and after 30 hours, a blister formed; after an application lasting 30 minutes the results were similar but more intense.

SUPERPALITE AND INTERMEDIATES

METHYLCHLOROFORMATE¹⁵ (CH3COOCH3)

The toxic concentration of this gas for mice for an exposure of 30 minutes was 1.2 mgm. per liter, or 276 parts per million. In high concentrations (24 mgm.) the mice immediately rubbed the nose and within a few minutes became dyspneic. Dyspnea progressed; they gasped wildly, while their eyes protruded. This was followed by convulsions and death. In concentrations of 4 mgm. the eyes were closed almost at once, but were opened again during the severe dyspnea which followed in the course of 2 to 3 minutes. At this concentration some of the mice died in convulsions in the gas chamber, while others with their feet spread, gasped in deep labored respiration, the expiration being accompanied by a sharp clicking sound, and death ensued in about an hour. In concentrations of 1.5 mgm. mice almost at once began to show signs of depression, during which they lay in the cage with deep respiration, their eyes partially closed. At this time there was a slight salivation, sometimes accompanied with a lacrymal discharge. Soon after gasping began, which continued till death, some hours later. In smaller concentrations the signs were somewhat similar, but the dyspnea was less intense. Although they gasped while exposed to the gas this ceased on removal.

CHLORMETHYLCHLOROFORMATE¹⁶ (ClCO2CH2Cl) (PALITE OR "K-STOFF")

Its physiological effects were very similar to those of phosgene; it was heavier, less easily dissipated, and so was better suited for employment in shells. In fairly high concentrations death occurred soon; low concentrations caused delayed effects exactly similar to phosgene. The delay was often protracted, deaths having occurred after intervals of from 10 to 15 days.

ACTION ON ANIMALS

Rat.—An exposure of 1 to 1,000 (5.76 mgm. per liter) for 1 hour caused death 2 hours later. A concentration of 1 to 2,000 caused death within 12 hours.

Cat.—After an exposure of 1 hour to a concentration of 1 to 1,000 the animal was very ill, with dyspnea and slow, prolonged inspiration. The lungs, upon

death, were edematous and congested. In a concentration of 1 to 5,000 there was marked lachrymation, but the respiratory effect was noticeable only toward the end of the hour. About 2 hours after release from exposure to the gas severe dyspnea and convulsions were in evidence. The animal died during the night, with lungs congested and edematous. A concentration of 1 to 20,000 produced lachrymation, salivation, and coughing. After 24 hours the animal was apparently well, but after 45 hours some bronchitis was present. In a concentration of 1 to 100,000 the animal showed lachrymation and some respiratory irritation. It was quite well two days later.

Dogs.—The minimum lethal concentration for dogs exposed for one-half hour is 1 to 6,000 (0.96 mgm. per liter), the animals dying in 24 hours. In a concentration of 1 to 3,000 the dogs died in about 12 hours.

EFFECT ON MAN

A concentration of 1 to 100,000 caused slight lachrymation and 1 to 200,000 was extremely irritant but could be respired by a resistant subject. In two observers this strength became irrespirable in 3 and 10 minutes, respectively, owing to cough and irritation. The toxicity was probably of the same order as that of phosgene.

TRICHLORMETHYLCHLOROFORMATE¹⁷ (Cl_3CCOCl) (SUPERPALITE OR DIPHOSGENE)

The toxicity of this gas for different species of animals was as follows:

ACTION ON ANIMALS

Mice.—When exposed for periods of 10 minutes to concentrations of 0.5 to 13.5 mgm. per liter, death was caused in nearly all instances. The toxic concentration was found to be 0.2 mgm. per liter, or 25 parts per million. When exposed to the gas in higher concentrations the mice showed signs of local irritation, a slight lachrymal and nasal secretion developing, a severe dyspnea then followed, and the animal died. In smaller concentration the signs were similar but less pronounced.

Cats.—Cats appeared to be more sensitive to this gas than dogs; for while dogs survived a concentration less than 0.30 mgm. per liter, the cats exposed to 0.2 and 0.11 mgm. per liter all died in 24 hours or less.

Other experiments gave results as follows:

Concentration	Exposure	Result
1-40,000 (0.221 mgm. per liter).....	1 hour.....	Sick for 2 days; recovery.
1-20,000 (0.442 mgm. per liter).....	do.....	Death in 12 hours.
1-7,000 (1.26 mgm. per liter).....	15 minutes.....	Death in 6 hours.
1-7,000 (1.26 mgm. per liter).....	5 minutes.....	Death in 48 hours.

Death is due to lung edema.

Rabbits.—With these animals the following results were obtained:

Concentration	Exposure	Results
1-27,000 (0.33 mgm. per liter).....	30 minutes.....	May die within 24 hours to 3 days.
1-20,000 (0.442 mgm. per liter).....	do.....	Die in 24 hours.

Dogs.—A summary of a series of experiments with dogs is given in Table 47.

TABLE 47.—*Toxicity of diphosgene on dogs*

Number of dogs exposed	Time of exposure (minutes)	Concentration of gas (milligrams per liter)	Deaths	Toxic concentration (milligrams per liter)
6	7½	2.13 -3.10	5	-----
10	7½	1.28 -1.68	4	-----
10	7½	.95 -1.11	6	-----
6	7½	.65 - .88	0	1.10
15	15	.39 -1.14	6	.78
16	30	.18 - .43	9	.36
16	60	.08 - .23	10	.15
11	120	.025- .13	6	.08
14	240	.026- .09	7	.046

The symptoms during exposure (7.5 minutes) were immediate excitement and irritation of the eyes and nose. Within a minute the animals usually quieted down and became drowsy and depressed. Salivation and lacrymation were profuse. Toward the end of the exposure the dogs were very drowsy, respiration was irregular and almost shallow. Frequently there was paling of the mucous membrane of the mouth. Soon after exposure the dogs had sore eyes, increased nasal secretion, and were generally depressed. Within 24 hours they developed a cough with labored and painful respiration. This condition persisted for from 5 to 25 days or longer. Death occurred anywhere from a few hours to 20 days after exposure.

After an exposure of 4 hours to a concentration from 0.046 to 0.09 mgm. per liter the symptoms observed were at first irritation of the eyes and nose, lacrymation and increased nasal secretion, salivation, frequently retching and vomiting, and occasionally defecation. The animals were usually drowsy and depressed before the end of the exposure. Later symptoms included depression, loss of appetite, sore eyes, cough, and labored respiration. This condition lasted for a period of from 1 to 13 days or longer. The deaths occurred usually in from 1 to 2 days, although one was delayed for 13 days.

Miller¹ studied the effect of repeated exposure to superpalite upon dogs. Twenty-one dogs that had been previously gassed with superpalite and had recovered were then reexposed; seven of them at a concentration of about 0.78 mgm. per liter, and the remaining 14 at concentrations varying from 0.40 to 0.62 mgm. per liter. The result was that 6 of the 7 exposed to the lethal concentration died. Only 6 exposed to the lower concentrations died, which is about what would have happened if fresh dogs had been subjected to the same conditions. After three weeks, the surviving dogs were again gassed, part to the lethal concentration and part to a lower concentration. The results were similar to those obtained in the first gassing. Four out of six exposed to the higher concentration and 2 of the 10 exposed to the lower concentration died. This procedure was continued until only 6 dogs were left.

From these results it seems probable that the susceptibility of dogs to superpalite was neither materially increased nor lessened by repeated exposure to sublethal concentration.

Sherwood and Snyder² investigated the smallest concentration that can be detected by the nose, mouth, and respiratory tract. The tests summarized in Table 48 were interrupted when the subject began to cough.

TABLE 48.—*Effect on the respiratory tract of different concentrations of diphosgene*

Milli-gram per liter	Parts per million	Number of tests	Irritation of throat, positive (per cent)	Cough, positive (per cent)	Irritation of lower respiratory tract, positive (per cent)
0.005	0.59	9	22	0	0
.008	.93	10	30	20	20
.013	1.52	9	67	56	11
.025	2.81	11	91	82	0

A concentration of 1.52 parts per million (0.013 mgm. per liter) caused throat irritation of almost all the subjects, and 2.81 parts per million (0.025 mgm. per liter) caused coughing in 82 per cent of cases.

Experiments were conducted to ascertain what concentration could be breathed without breaking down in about 3 minutes, and 16 subjects were tested with results as follows.

Breathing by the mouth only, eyes protected:

Concentration	Number breaking down
1-500,000 (0.0176 mgm. per liter)-----	2
1-333,000 (0.0265 mgm. per liter)-----	8
1-250,000 (0.0354 mgm. per liter)-----	3
1-200,000 (0.0442 mgm. per liter)-----	1
1-166,000 (0.053 mgm. per liter)-----	2

Breathing by the nose, eyes unprotected:

Concentration	Number breaking down
1-500,000-----	2
1-333,000-----	6
1-250,000-----	5
1-200,000-----	3

ACROLEIN ¹⁸ ($\text{CH}_2=\text{CHCHO}$)

Acrolein is a lacrymator and respiratory irritant; the effects on the eyes and throat occur simultaneously. In concentrations of 0.025 mgm. per liter it induces secretion of saliva, lacrymation, nasal secretion, and slight narcosis.

ACTION ON MAN

One part in 200,000 acted as a lacrymator and nasal irritant, while 1 part in 100,000 was intolerable. The minimum effective concentration with or without eye protection was 1 to 100,000 (0.025 mgm. per liter). The toxicity was about the same as phosgene.

ACTION ON ANIMALS

Mice.—At an exposure of 10 minutes the immediate toxic concentration was between 0.55 and 0.38 mgm. per liter. This killed more than 50 per cent of the mice within 48 hours. The delayed toxic point (that which killed after 48 hours and in less than 10 days) was between 0.16 and 0.17 mgm. per liter. In concentration of 1 mgm. or more there was increased excitement but lower concentrations produce depression. All concentrations caused irritation as shown by rubbing of the nose and closing of the eyes. Gasping was also a constant symptom, it being only occasional with the low concentrations but continual with the highest concentration, namely, 4 mgm. per liter. The delayed deaths took place in from 48 to 65 hours.

With concentration of 4.1 mgm. per liter all 4 mice died within 7 minutes. They showed violent excitement from the onset and died with convulsions. Moderate concentrations killed all within 1 to 46 hours.

Rats.—One part in 1,000 killed in 50 minutes.

Cats.—A dose above 0.04 mgm. per liter caused such intense irritation that some days were required for recovery. With 0.2 mgm. per liter the lung-irritation phenomena were not recognizable, but were obviously painful, and the muscles came into activity. A dose of 1.5 mgm. per liter seriously affected the animal, which died after 2½ hours' exposure to the gas of lung edema and hemorrhage of the lungs; with a dose of 1.98 mgm. per liter death resulted 2.5 hours later.

Dogs.—The dogs were very much excited during the early part of the exposure. The eyes and nose were at once irritated and the animal blinked and licked his nose the instant the gas was turned on. Lacrymation and salivation were both profuse. After a short time the animals kept their eyes tightly closed. The cornea was usually dulled. Nasal secretion was very much increased. Respiration was early affected, becoming very slow and labored. Toward the end of the exposure the animal was usually much depressed. Within a few hours after exposure the animal developed a severe tracheal rattle, was very depressed, coughed, and had labored respiration. With toxic concentrations death occurred in four hours to two days. With nontoxic concentrations the animal was very sick for several days and did not recover completely for a week or more. The toxic concentration might be placed at 0.35 mgm. per liter.

SENSITIVENESS OF INDIVIDUALS

Experiments to determine the smallest concentration of acrolein that could be detected by the eyes, nose, throat or lower respiratory tract showed that acrolein was detectable by its odor at a concentration of 0.0028 mgm. per liter or 1.12 parts per million and that some individuals could detect it at even smaller concentrations. When the amount of gas was increased to 0.0077 mgm. per liter (3.06 parts per million) irritation of the eyes and nose became a prominent symptom in the majority of tests. Lacrymation did not become pronounced until the concentration reached 0.010 mgm. per liter or 4 parts per million.

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- (11) *Ibid.*: Vol. XXI, Part I, Chapter X, April, 1919.
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- (14) *Ibid.*: Vol. XXI, Part III, p. 182, April, 1919.
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- (16) *Ibid.*: Vol. XXV, Chapter III, March, 1919.
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- (18) *Ibid.*: Vol. XXIX, Chapter I, May, 1919.

^a The monographs cited are based on official documents on file in the office of the Chief, Chemical Warfare Service, Munitions Buildings, Washington, D. C., or in the Medical Research Division, Edgewood Arsenal, Md. All monographs on file, Medical Research Division, Edgewood Arsenal.

CHAPTER XIV.

EXPERIMENTAL PATHOLOGY OF WAR GASES, EXCLUSIVE OF MUSTARD GAS^a

The investigations herewith presented were carried out in 1917-18 in the laboratories of Yale University, New Haven, Conn., and American University, Washington, D. C., under the direction of the medical science section of the Chemical Warfare Service.^a These investigations had their inception in studies on the general problems of war gases, begun in 1917 by the Bureau of Mines of the Department of the Interior, and later transferred to the newly organized Chemical Warfare Service. The scope of the work widened so rapidly that a division into the separate fields of physiology, pathology, and therapy was deemed advisable. The studies in pathology, with which this chapter is concerned, were under the direction of Maj. M. C. Winternitz, M. C., professor of pathology, Yale University.

At the Yale station the work was done chiefly in the Brady Laboratory of Pathology and Bacteriology, in close collaboration with the department of physiological chemistry, which had charge of investigations on physiology and therapy. At American University there was similar cooperation between the pharmacologists and pathologists, thus making possible at each institution the investigation of a large amount of material.

In order to avoid duplication of effort the two stations took up the study of different groups of gases. At the Yale station chlorine, chloropierin, and phosgene were investigated; at American University arsine, organic arsenicals, superpalite, cyanogen compounds, and mustard gas were studied. Special problems relating to the effects of these gases were similarly assigned. Unfortunately, from the scientific standpoint, the work ended rather abruptly on December 1, 1918, leaving unfinished the solution of a number of problems.

CHLORINE

Chlorine, first of the toxic gases used in the World War, was among the first to be subjected to experimental study by the Medical Division of the Chemical Warfare Service. In the course of the pharmacologic and therapeutic studies upon this gas, carried on in Washington and New Haven, the results of which are discussed elsewhere in this volume, animals in large numbers were gassed, thus providing abundant material for pathologic investigation.

In these studies the dog was the experimental animal of choice, although, as with other gases investigated, various other animals (guinea pigs, rats, mice, rabbits, cats, monkeys, and goats^b) were used by way of comparison. The reason for using the dog is that, in the study of the respiratory irritant

^a The data in this chapter are based on reports prepared under the direction of Maj. M. C. Winternitz, M. C., and published as: "Collected Studies on the Pathology of War Gas Poisoning," New Haven, Conn., Yale University Press, 1920.

^b The goat as an experimental animal was preferred by some British investigators, partly because of the larger size and distinct lobulation of the lungs, and also because of the resistance of this animal to infection, which permitted a better study of the uncomplicated gas injury. In the conduct of the investigations here discussed the very large size of the lungs was not believed to be an advantage; and the fact that in their relative immunity to respiratory infection goats differ markedly from man was believed to be a reason against rather than for their use, except in so far as the absence of infection permitted the study of uncomplicated gas injury.

gases, to which group the majority of war gases belong, this animal has certain well-recognized advantages: (1) The lungs and other organs are sufficiently large to make gross examination easy. (2) Anatomically the respiratory tract resembles closely that of man. (3) The conditions of pulmonary infection and the reaction of the lungs to bacterial and other injuries are much the same as in human beings.

The accompanying diagram (Fig. 46) shows very well the topography of the dog's respiratory tract. The trachea is considerably longer than the human organ, but it branches in similar manner, as shown in the diagram. As in

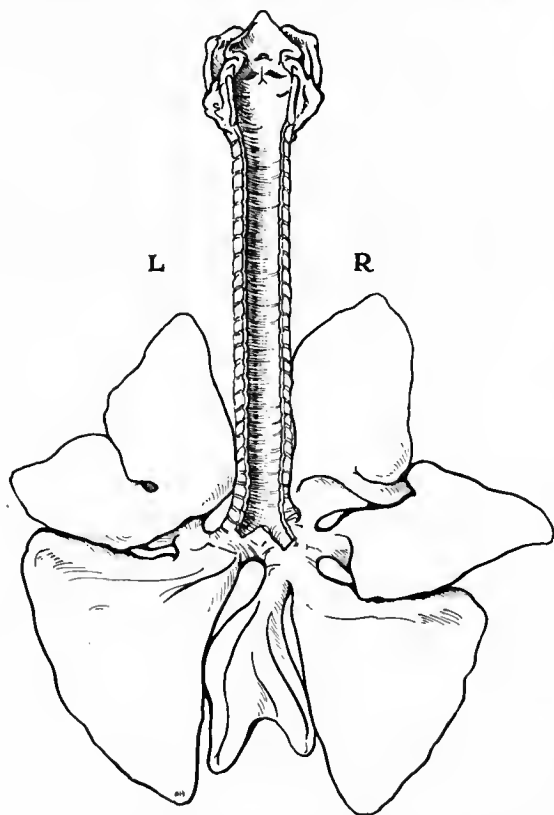


FIG. 46.—Diagram of dog's respiratory tract viewed from behind. The interlobular fissures and the accessory caudate lobe are well shown

man, the right lung has three lobes and the left two. The divisions are more complete, however, and the left upper lobe has a deep fissure, nearly dividing it into two equal parts. There is a sixth, or caudate, lobe which, as the diagram shows, may be considered as belonging to the right lung, although its bronchus is given off close to the tracheal bifurcation, and its position behind the pericardium is rather neutral.^c

The relations of the bronchial tree are shown very well in Figure 47. It is a fact of interest and importance, as the succeeding report will show, that the respiratory irritant gases exhibited striking differences in their action on the several segments of the air passages: Mustard gas, for example, damaged chiefly the first portion—that is, trachea and large bronchi; others, such as phosgene and super-

palite, affected only the distal portion; while chlorine, the gas under consideration, injured the entire tract.

The material upon which the present report is based includes 326 dogs that succumbed or were killed after exposure to chlorine in gassing chambers. The time of exposure was in most cases 30 minutes; the concentration varied between 600 and 1,100 parts per million.

^c In considering the pathological anatomy and physiology of the lung of the dog or other quadruped, it should be kept in mind that the anterior portion of the organ and not the so-called lower or diaphragmatic portion, as in man, is the most dependent in the normal posture of the animal. The significance of this fact will be discussed in connection with the localization of certain of the lesions following gassing.

AUTOPSY FINDINGS

While death following severe exposures often occurred within a few minutes and was generally not delayed beyond a few hours, the exposed animal might survive the acute period, only to succumb after days or even weeks. As might be expected, the pathological changes found at autopsy varied markedly with the period of survival, and it will make for clearness of description if in the discussion of these changes, the cases studied are divided into three groups: (1) Acute deaths; (2) delayed deaths; (3) chronic or recovered cases.

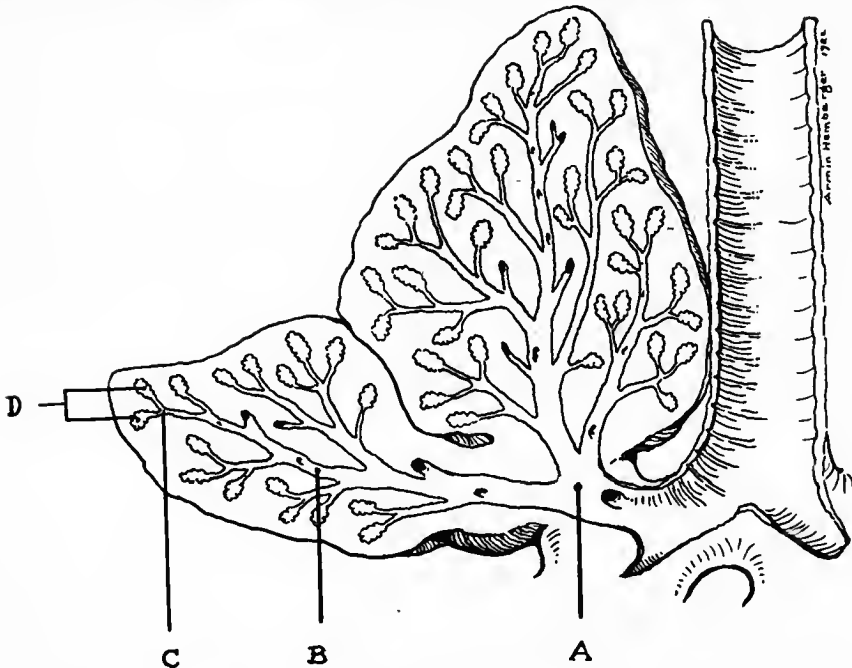


FIG. 47.—Diagram of bronchial tree of dog, showing bronchi of first, second, and third order (A, B, C) and infundibula (D)

In Table 49 the animals are grouped according to the duration of life after gassing. It is seen that a majority of the fatalities occurred in the first 24 hours, 172 out of 270, or 64 per cent. When figures are plotted (Chart XXIV) it is also seen that the death curve starts with a sharp rise, which is followed by an equally sharp fall. There is a short secondary rise on the fourth day. This second rise, it is believed, is to be attributed to the development of pulmonary infection, a phenomenon that will be emphasized in a succeeding paragraph.

TABLE 49.—Dogs gassed with chlorine

Dogs dying—	Autopsied			Dogs dying—	Autopsied		
	Died	Killed	Total		Died	Killed	Total
Group I:				Group III—Continued.			
First 12 hours.....	62	3	65	Tenth day.....	2	—	2
12 to 24 hours.....	110	—	110	Eleventh day.....	2	—	2
Group II:				Twelfth day.....	1	—	1
Second day.....	25	—	25	Fourteenth day.....	1	—	1
Third day.....	8	—	8	Group IV:			
Fourth day.....	13	—	13	Fifteenth to thirtieth			
Group III:				day.....	11	8	19
Fifth day.....	7	—	7	Thirtieth to one hun-			
Sixth day.....	4	—	4	dred and ninety-			
Seventh day.....	4	—	4	third day.....	15	45	60
Eighth day.....	2	—	2	Total.....	270	56	326
Ninth day.....	3	—	3				

ACUTE DEATHS

GROSS FINDINGS

The gross changes seen at autopsy, when death occurred in the first 24 hours after gassing, were remarkably uniform. Such differences as were noted were largely those of degree. In general it may be said that the changes, particularly in the respiratory system, became progressively more marked as death was delayed, up to 24 hours, when the acute, uncomplicated lesions had reached their maximum.

As a rule, the eyes were reddened, showing an acute conjunctivitis, with a serous or seropurulent discharge. A frothy fluid exuded from the mouth, and if the body had lain unmoved for several hours, a pool of coagulated fluid was seen about the head. Post-mortem changes were conspicuous even within

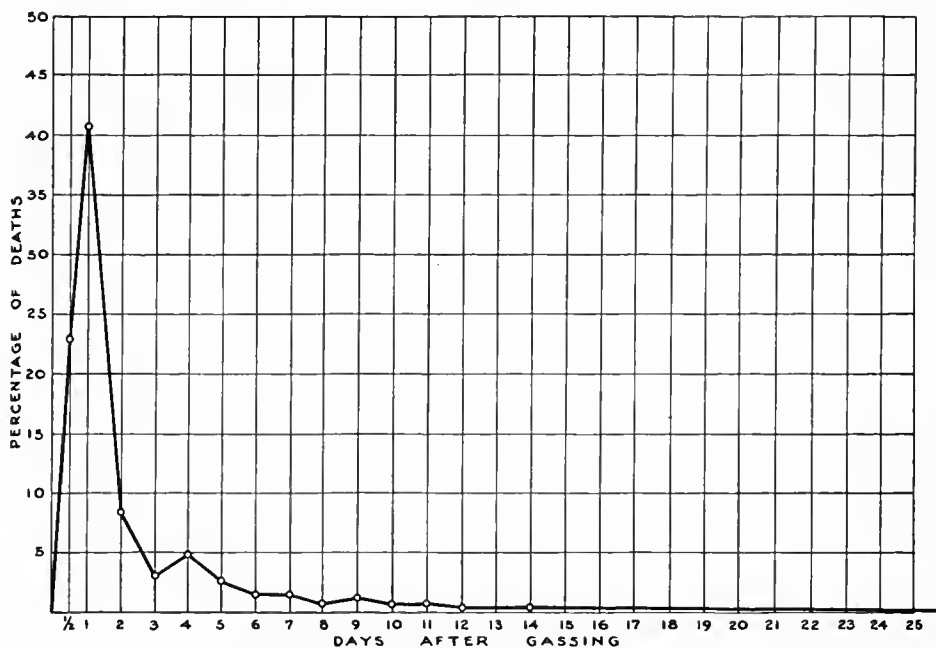


CHART XXIV.—Duration of life after chlorine gassing

3 to 4 hours after death, and decomposition could be quite advanced after 5 or 6 hours. An invasion of the tissues by the gas bacillus was often seen, and the liver, even after only 2 or 3 hours, was at times mottled with gaseous foci of varying size. That autolytic processes proceeded more rapidly after death in gassed than in nongassed animals seemed very evident, although no careful or systematic observations were made regarding the phenomenon, which was apparently an acceleration of the normal autolytic processes.

The abdominal organs showed a pronounced congestion, which was particularly striking in the liver. The congestion was less marked in the kidneys and spleen. The vena cava and its larger branches were distended. This splanchnic engorgement undoubtedly was dependent upon disturbances in the pulmonary circulation, discussed below.

On opening the thorax, the voluminousness of the lungs, which tended to overlap in the median line was very striking. The pleural surface did not show

the usual wrinkling of the normally collapsed organ, but was tense, glossy and semitranslucent. The tissues in the anterior mediastinum, including the areolar tissue about the thymus and the great vessels were markedly edematous.

The heart was quite regularly distended with blood; sometimes markedly so. Occasionally the apex was bifid and the tip of the right ventricle might project further than the left. All chambers of the heart shared in this apparent dilatation, but the right ventricle seemed most affected. If the animal was autopsied immediately after death, the blood was fluid, but clotting took place rapidly, with the result that the clots were generally of the dark cruor type. This was true, particularly, of animals that had survived gassing only a few hours. Where death was delayed more than 12 hours, the clots were more often of the usual chicken-fat quality, indicating less rapid coagulation. The endocardium, as a rule, was quite smooth and pale, but occasionally on both the valvular and mural endocardium brilliant flame-like hemorrhages were found which might be irregularly stellate or rounded in form. Very rarely the endocardium over these hemorrhages was roughened and, in a single instance, a large thrombus was attached to such an area in the region of the tricuspid valve.

As the trachea and bronchi were opened, a quantity of frothy fluid poured out. The mucous membrane of the trachea was reddened and the vessels were deeply injected. In animals surviving only a few hours, the surface was quite smooth, though somewhat opaque, with a loss of the normal gloss and translucency. Later the surface was covered by a sticky, membranous exudate which was quite tenacious, and was removed with difficulty. The gross appearance of the larger bronchi was practically identical with that of the trachea.

The lungs were very voluminous and retained their shape upon removal, even after considerable fluid had escaped through the bronchi. They collapsed slightly after sectioning, chiefly from the loss of fluid through the several bronchi. The tissue was more or less doughy throughout, with faint crepitation in places. The color was brilliant and variegated. The background was a red of deep, rich quality, with a mixture of blue, giving to the whole in general, a purple hue. There were lighter-colored patches, most numerous toward the margin of the upper lobes but scattered generally through all lobes. These paler areas were slightly elevated and were readily recognized as patches of emphysema, obviously compensatory, as in human lobar pneumonia. In some places the air of the distended vesicles had been replaced by fluid. Occasionally dark red depressed patches were seen, which clearly represented partially collapsed lobules.

When the lung was sectioned a tremendous amount of fluid escaped. The cut surface was red and more or less translucent. There was very little air in the bronchi and still less in the lung tissue proper. The escaping fluid was generally rich in albumin and might coagulate on standing. The larger blood vessels stood out prominently everywhere, owing to the presence about each of a relatively white edematous zone which might measure as much as 4 mm. in width. In animals dying within a few hours after gassing there was no gross evidence of an inflammatory reaction in the lung, other than the presence of the serous exudate just mentioned; but in animals that survived 12 to 24 hours small areas of pneumonic consolidation were sometimes recog-

nizable with the naked eye, although with difficulty, owing to the coexisting edema and congestion which obscured the picture. A well-developed pneumonia was not often seen in the first 24 hours.

MICROSCOPIC FINDINGS

In the respiratory tract, where practically the only changes of importance were found, histological examination not only confirmed at once the gross

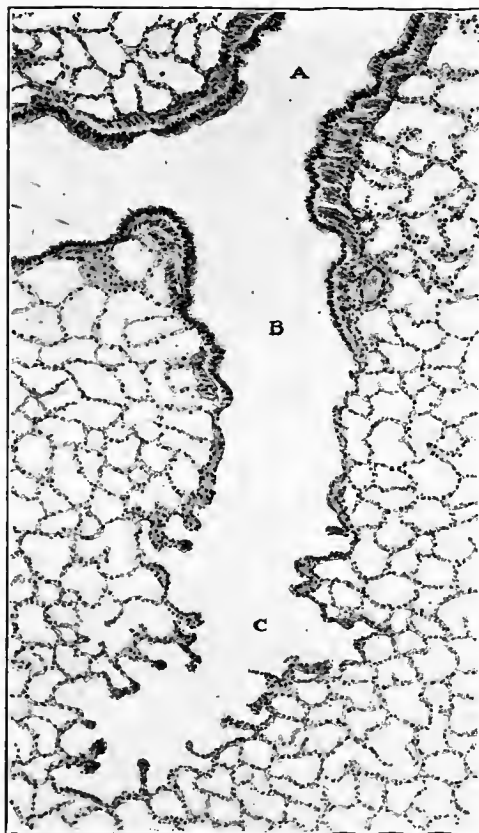


FIG. 48.—Normal bronchus. Bronchiolar termination in a dog's lung, showing transition from high ciliated epithelium of bronchi to the flattened epithelium of the infundibula

findings in the way of necrosis of tracheal epithelium, pulmonary edema and congestion, focal emphysema and atelectasis, but it also threw some light on the mechanism of the development of these lesions.

The changes in the epithelial lining of the respiratory tract, which were undoubtedly fundamental, will be considered first. (Fig. 48.) The mucosa of the trachea and bronchi, even in cases of death in two hours after exposure, looked completely coagulated. (Fig. 49.) The nuclei were pycnotic and the cytoplasm homogeneous and glassy. The membrane was often raised in blisterlike fashion from the submucosa, and sheets of it were found lying in the trachea and bronchi. (Fig. 50.) It soon began to slough, and fragments free in the lumen underwent rapid disintegration. This epithelial necrosis was clearly seen even in the smallest bronchi, but in the atria and air vesicles the damage to the inconspicuous lining cells was not so evident, although there was more or less desquamation.^d

A thorough examination of the lung showed that the damage was not limited to the destruction of the lining epithelium, but that in many instances foci of hyaline necrosis of the entire alveolar wall were found. (Fig. 51.) These focal necroses varied in size, but generally comprised a group of air vesicles

^d In order to determine the extent and rapidity of the damage to the epithelium, resort was made to the use of vital stains, which, as is well known, serve to distinguish dead from living cells, before catabolic changes have taken place, no such distinction being possible by ordinary staining methods. Dogs were given appropriate doses of trypan blue intravenously, and after a proper interval were subjected to a lethal exposure of chlorine. Some were killed shortly after gassing; others died within 24 hours. In all cases examination of the respiratory tract showed an intense nuclear stain, not only of the lining cells of the trachea and bronchi, but also of much of the flattened alveolar epithelium, particularly that about the atria. From these observations it was concluded that chlorine acted directly on the respiratory epithelium and that cell death immediately followed exposure. With this action of the gas clearly in mind, many of the other pathological phenomena, particularly the bacterial invasion and the associated massive inflammatory reaction, became readily explicable, as will be emphasized in the subsequent discussion.

which in some sections were seen to open into a common bronchiole. (Fig. 52.) The alveolar walls were homogeneous, glassy, and stained deep pink in hematoxylin-eosin preparations. In our experience this lesion was not associated with any other gas than chlorine. In a careful study of the lungs, in 50 acute deaths from chlorine, areas of necrosis were demonstrable in all but 3, and in these only two sections from each case were examined. It would appear then that the association of the lesion with chlorine was sufficiently constant to make its presence of considerable differential diagnostic value in warfare where the type of gas used is not always known.

The pulmonary capillaries, as the gross picture indicated, in most places were engorged with blood. This was particularly true in the partially collapsed areas. In general, the content of the vessels was not obviously altered. The leucocytes were sometimes slightly increased in places, but this was not marked. Thrombi in the pulmonary vessels have been described by several investigators, including Klotz¹ and Bunting, but in the studies here recorded it was not satis-



FIG. 49.—Bronchus plugged with sloughs of "cooked" epithelial lining. The cytoplasm of the cells is quite homogeneous and hyalinized

factorily determined that in dogs, at least, definite thrombi were present, either in the capillaries or larger vessels, nor was it clear that the picture which Klotz described was sufficient evidence of antemortem coagulation. With special stains, however, it was possible to demonstrate, in many cases, a thick layer of fibrin covering the alveolar wall, and in places fibrin strands crossing the capillary to the alveolar surface of the adjacent air chamber. Presumably these fibrin deposits were laid down in the course of the outpouring of plasma from the capillary into the alveoli; in other words, the plasma coagulated partially or completely as it exuded. It was not only conceivable but very probable that such a coagulum would impede the flow of blood through the capillaries, even if it did not lead to intra vitam clotting, as Klotz¹ maintained. The blood in the larger vessels of the lung looked normal and the intima and media of the vessels were unaltered. The adventitia, however, was in many cases strikingly edematous and the perivascular lymphatics, as Edkins and Tweedy²

have emphasized, in their experiments with rabbits, are markedly distended. Occasionally, the edema of the perivascular sheath was replaced by blood, resulting in a circular, ring-like hemorrhage.

The outpouring of fluid not only into the air sacs of the lung but also into the tissue spaces of the tracheal, bronchial, and alveolar walls constituted both grossly and microscopically, as it did clinically, the dominant feature of the pathological picture. In some cases the pulmonary alveoli were filled with the precipitated pink-staining fluid, making the organ resemble superficially the thyroid with its colloid-filled vesicles. The fluid varied in its albumin content, as indicated by the slight precipitation in some cases. This variation might

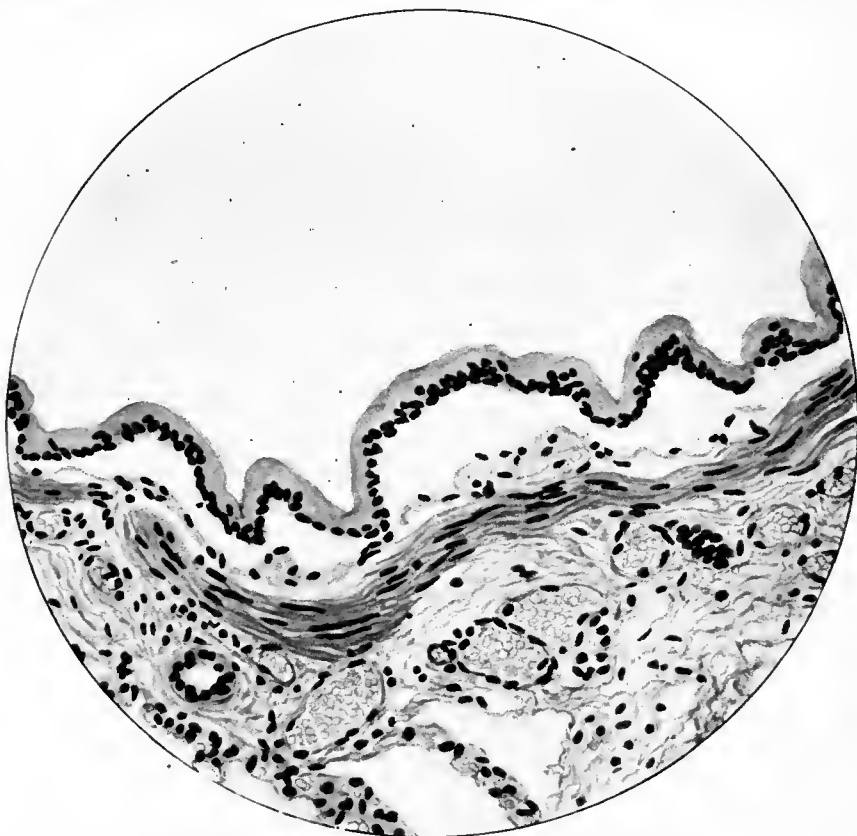


FIG. 50.—Higher magnification of necrotic lining shown in Figure 49

be due to the stage of the edema, the fluid coming out first being, according to Klotz,¹ poor in albumin, or it might depend on the degree of permeability of the damaged alveolar walls. The interstitial tissue, as well as the air sacs, was filled with fluid. The adventitia of the larger blood vessels was usually strikingly edematous, with a dilatation of its lymphatics. (Fig. 53.)

In addition to the edema there were seen quite early scattered mononuclear cells in the alveoli. These were for the most part desquamated epithelium, but there were a few mononuclear and polymorphonuclear leucocytes. In a certain number of cases there were accumulations of polynuclears, particularly in and about the atria, giving the picture of an early pneumonia. (Fig. 54.) It is a question as to whether this focal reaction was due to the gas injury or to invad-

ing pathogenic bacteria. This question will be discussed in a subsequent paragraph, but it may be stated here that the investigations tended to show that once the protective epithelial barrier was destroyed, bacteria entered the lung almost immediately and that these focal reactions were undoubtedly the results of such invasion.

DELAYED DEATHS

Reference to Chart XXIV shows that of the animals which came to autopsy 172 died during the first 24 hours, 25 on the second day, and 8 on the third day. These figures emphasize the fact that the bulk of the fatalities occurred during the first 24 hours, but it is obvious that any line of division between these acute deaths and what may be termed delayed deaths must be quite arbitrary.

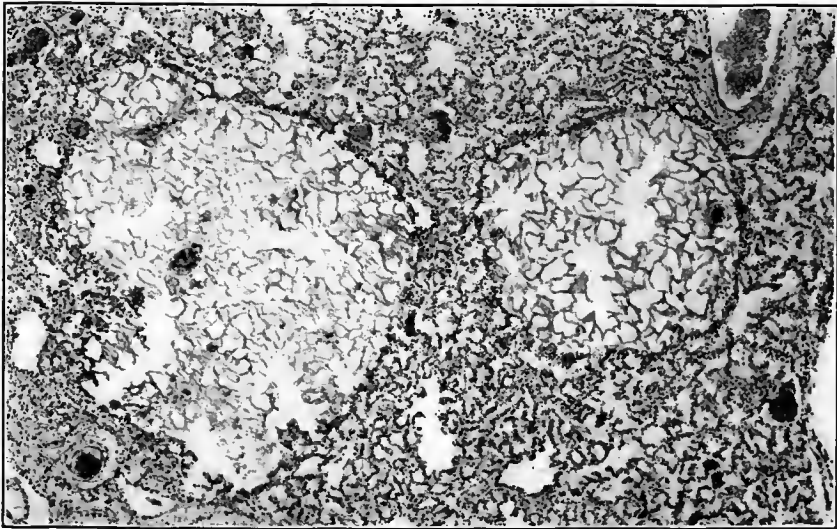


FIG. 51.—Multiple areas of focal necrosis in lung of dog dying 20 hours after chlorine gassing

Certainly as regards pathologic findings, there was no abrupt transition. Furthermore, among animals dying in the first 24 hours, pneumonia, if present, was seen only as an early lesion, entirely obscured by edema and congestion, whereas in the later deaths there was a well-marked pneumonia in at least 95 per cent of the cases. There is here, therefore, a fair basis of division.

TABLE 50.—*Dogs gassed with chlorine*

	Per cent showing pneumonia				Per cent showing bronchitis and bronchiolitis			
	All types	Early	Ad- vanced	Organ- izing	All types	Early	Ad- vanced	Organ- izing or obliterative
Dogs dying:								
First 12 hours.....	18	18			36	36		
12 to 24 hours.....	54	26	28		56	27	29	
2 to 4 days.....	95	26	65	4	61	13	48	19
5 to 14 days.....	100		11	89	69		50	8
15 to 30 days.....	83	8	23	52			17	10
31 to 193 days.....	24		7	17	10			
Dogs killed:								
15 to 193 days.....	24		7	17	51		17	34

As might be expected, the pathological findings in these delayed deaths showed a greater variation than was noted in the acute cases. The time factor, of course, was important. In animals dying 2 to 4 days after exposure, the pulmonary edema and congestion which reached its maximum during the first 24 hours was still present to a marked degree, though it might be on the decline. Pneumonia, as stated above, was practically always present. Grossly, it may be either of the lobar or lobular type, but if the former, the appearance suggested a confluent lobular rather than a true lobar process. The relation of the bronchi to the patches of consolidation was usually quite evident. Histologically, there

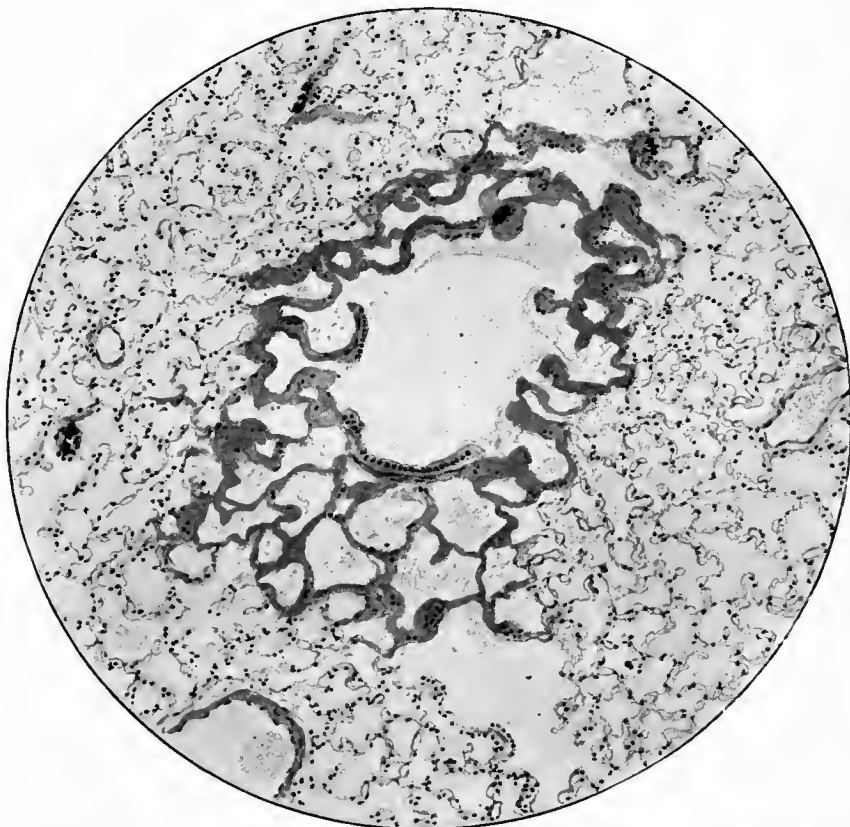


FIG. 52.—Higher magnification of an area of focal necrosis such as is shown in Figure 51. Death occurred six hours after gassing. The alveolar walls about an atrium are completely hyalinized and stain deeply with eosin

were special features of the pulmonary and bronchial lesions which had a certain resemblance to the changes found in the lung in epidemic influenza. There was, for example, the same striking degree of injury of the bronchial wall, and the focal hyaline necrosis of the alveoli. There was also, as in influenza, an active regeneration of the respiratory epithelium which was seen not only in the alveoli but even more strikingly in the bronchi. As previously described, the gas destroyed the ciliated epithelium of the trachea and bronchi. There was left, however, the deeper syncytial layer, the cells of which might be seen in an active state of multiplication as early as 48 hours after gassing, and the process became still more active after 4 or 5 days. Several mitotic figures might be found in a

single field. In the smaller bronchi, however, the distribution might be so complete that even the deeper layer of epidermis was destroyed, and repair took place only by a new growth of connective tissue which filled the lumen and eventually obliterated it. (Fig. 55.) A widespread organizing pneumonia was not infrequent in animals living 5 to 10 days. Abscesses and small gangrenous cavities were also common complications. In some instances the gangrene evidently originated in foci of necrosis such as were described in connection with acute deaths, but in most cases the lesion was undoubtedly referable to the action of bacteria. Suppurative pleurisy was an infrequent complication.

CHRONIC OR RECOVERED CASES

In any large series of animals receiving an average lethal exposure to chlorine a certain percentage of recoveries will be observed. As Underhill

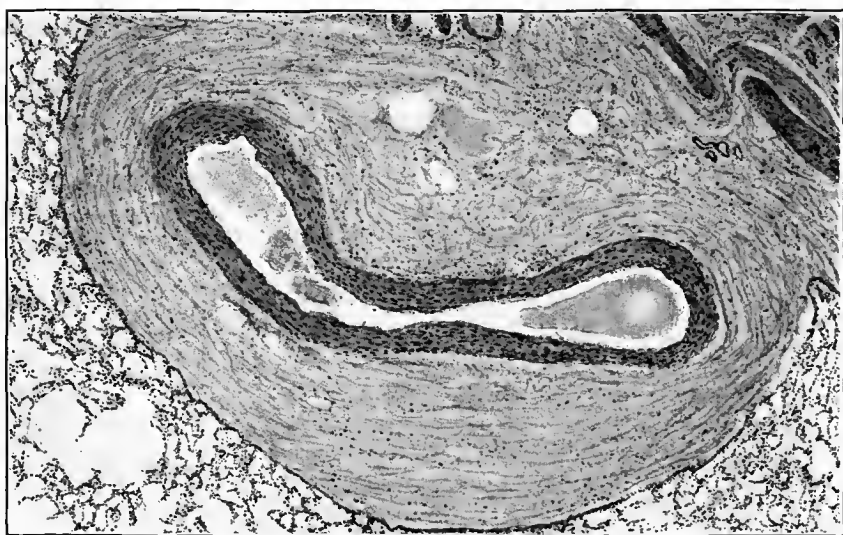


FIG. 53.—Marked perivascular edema in acute death from chlorine. The lymphatic channels of the adventitia are widely distended with fluid

and others have pointed out, this was true of practically all of the toxic war gases, and was due partly to individual variations in susceptibility and partly to the technical difficulty of insuring a uniform dosage for each animal. If the recovered animals were kept under observation it would be found that some died sooner or later as a result of changes referable directly or indirectly to the gassing, and that many of the others, if killed, showed secondary effects of the gas injury. The percentage of cases in which perfectly normal organs were found at autopsy in such a group of animals was relatively small. The following summary of observations in a large number of "recovered dogs" will serve to confirm the general conclusions just stated.

There were 79 dogs living 15 days after gassing. Of these, 26 died between the fifteenth and one hundred and ninety-third days, when the observations ended. Of these deaths, 11 occurred between the fifteenth and thirtieth day. The remaining 53 animals were killed, most of them between 3 and

6 months. In nearly all cases, a few days after gassing, the dogs were sent to a farm in the country, where they were kept until they died or were killed. Many of them looked to be in good health, but some were lean and sluggish, and began to cough when made to exercise freely. Those that died were poorly nourished, without exception, and a few were quite emaciated. All showed at autopsy well-marked anemia, moderate fat accumulations in the liver and kidneys, enlargement of the spleen, in addition to the chronic changes in the lungs, which will be described in some detail.

The lungs showed in some cases maroon-colored areas of partial or complete atelectasis, while the rest of the pulmonary tissue was irregularly emphy-

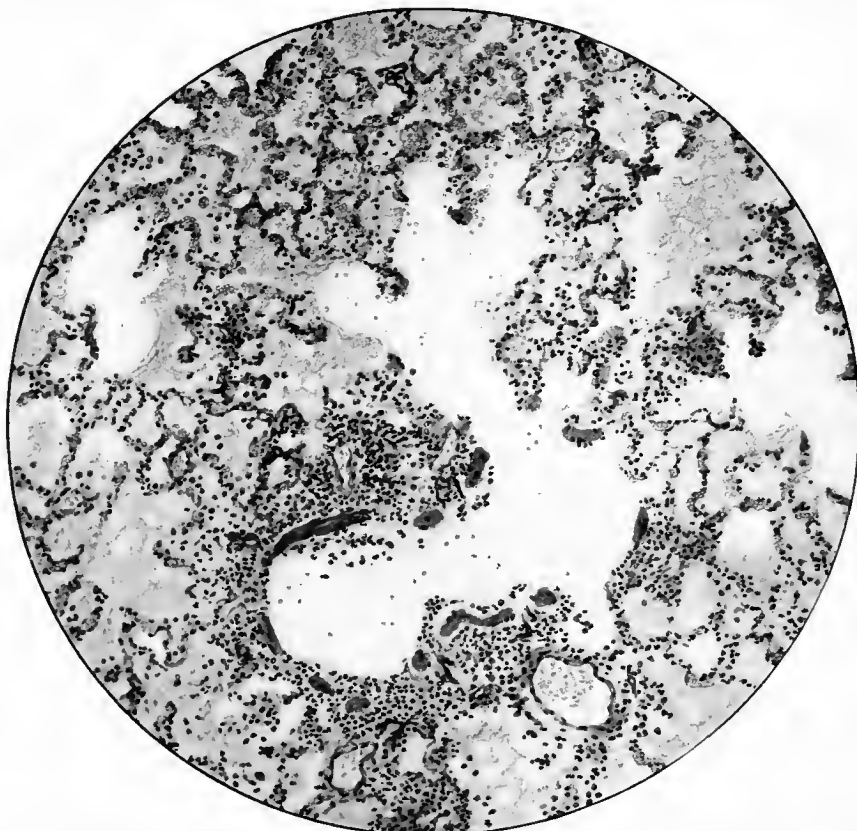


FIG. 54.—Early inflammatory reaction in the lungs found six hours after exposure to chlorine. The cells of the exudate are chiefly polynuclears which accumulated in and about an atrium

sematous. The atelectatic areas were associated quite regularly with gross changes in the bronchi leading to these parts. These changes were chiefly a thickening of the walls and plugging of the lumina, with a mucopurulent exudate. The extent of these changes varied in individual cases. Microscopically, the emphysema and atelectasis noted grossly were quite evident. The associated changes in the bronchi varied. In places there was a pronounced chronic infection, the lumen being filled with leucocytes and cellular debris. The mucosa and other coats were infiltrated by wandering cells and in some instances a wide mantle of cells in the adjacent lung tissue. (Fig. 56.)

Another and more characteristic lesion was found in the smaller branches of the bronchial tree. This was what might be termed an organizing or obliterative bronchiolitis. In the development of this lesion there was evidently first a partial and later a complete occlusion of the bronchiole. The lumen was first filled with an exudate composed of leucocytes, fibrin, and necrotic epithelium, as seen in some of the delayed deaths described above. This exudate became gradually organized through the ingrowth of blood vessels and fibroblasts from the bronchial wall. (Fig. 57.) A noncellular fibroid scar might finally result, or in some instances the organized mass might persist as a sort of polyp partly covered by epithelium. (Fig. 58.)



FIG. 55.—Organizing bronchiolitis five days after chlorine gassing. Lumen of bronchus is filled with a network of fibroblasts and there is a similar organizing process going on in the adjacent pulmonary alveoli. In the bronchial and alveolar walls there is much old hyalinized fibrin.

This partial or complete bronchial obliteration explained the presence of the patchy emphysema and atelectasis to which reference has already been made. It may be mentioned in passing that these chronic bronchiolar lesions were quite analogous to those observed in the human lung, as described by Wagner³ and others.

A considerable number of animals showed, in addition to the healed bronchial lesions, with resulting mechanical disturbances, evidence of a superimposed chronic infection. In these cases chronic bronchitis, bronchiectasis, and patches of organizing pneumonia were observed, the extent of the change

being dependent apparently on the type of infecting organism and the amount of initial gas damage, though of course the undetermined factor of individual resistance had to be taken into account. The character of the commoner bronchial lesions is shown very well in Figures 58 and 59. In a few instances, the infection had spread to the pleura with the development of a typical empyema, and there were several cases in which a generalized infection had taken place, with metastatic abscesses in the viscera. These instances of extensive infection, however, were exceptional, the usual picture being simply a chronic purulent bronchitis with more or less peribronchial reaction.

Routine gross and microscopic examination of various organs and tissues, including intestinal tract and brain, disclosed no chronic change of any significance. It seems reasonable, therefore, to assume that the poor general condition of the animals was referable to impaired pulmonary function, although it must be granted a much more exhaustive study of this question is necessary



FIG. 56.—Purulent bronchitis in a dog dying 23 days after exposure to chlorine. The cells in the bronchi are chiefly polynuclears, but in the adjacent alveoli are many large mononuclear cells

before any definite conclusion can be reached. The problem is clearly an important one in that its solution would throw light on the nature of the chronic disability seen in many of the recovered gassed soldiers.

SUMMARY

The inhalation of chlorine resulted in damage to the lining epithelium of the entire respiratory tract, the degree of injury depending upon the concentration of the gas and the duration of exposure. In lethal exposures, there was complete necrosis of the tracheal and bronchial mucosæ, with subsequent sloughing and focal necrosis of the pulmonary septa. When death occurred immediately, the injury was demonstrable by the use of vital stains; no inflammatory reaction was manifest. In deaths occurring a few hours after gassing, the initial injury was obscured by reactive phenomena, chiefly edema and congestion of trachea, bronchi, lungs, and interstitial tissues. Where death was further delayed, bacterial invasion of the damaged tissues occurred through

the loss of the normal protective mechanism of the upper air passages. This resulted in a widespread inflammatory reaction involving trachea, bronchi, and lungs.

There was no anatomical evidence of injury to tissues other than those of the respiratory tract. Dilatation of the heart and circulatory disturbances, when present, were undoubtedly secondary to the pulmonary lesions.

Animals recovering from severe exposures showed chronic changes in the lungs of the nature of organizing bronchiolitis, chronic bronchitis, bronchiectasis and emphysema. These changes were referable partly to the initial gas dam-

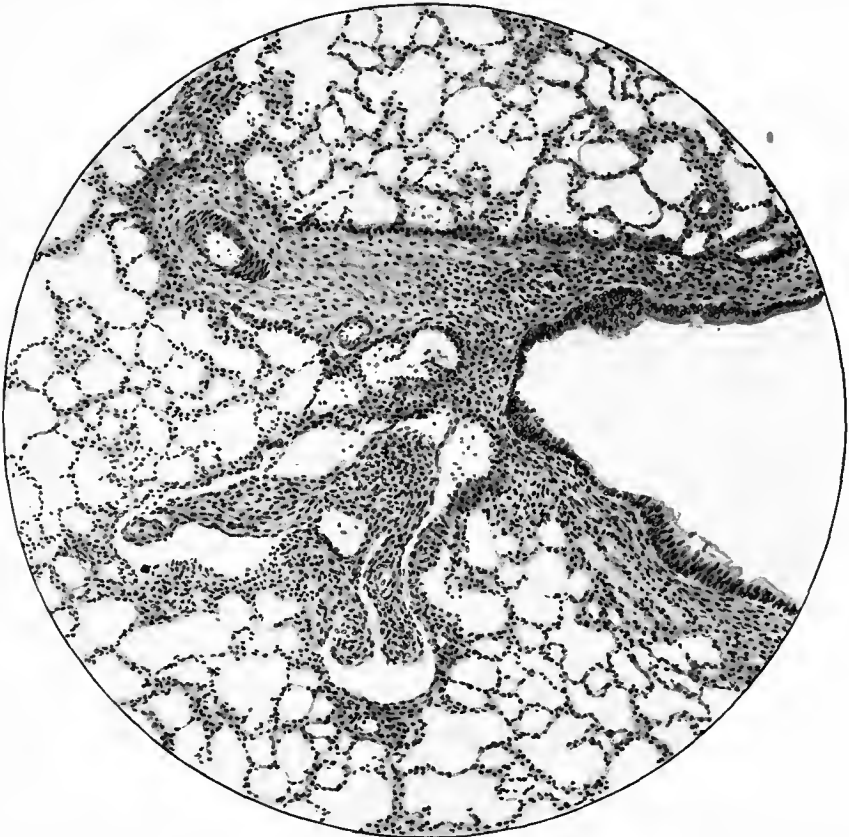


FIG. 57.—Obliterating bronchiolitis in a dog killed 32 days after chlorine gassing. The main bronchus has a normal, probably regenerated, epithelial lining. The small tributary bronchus is occluded by an organized mass of tissue adherent to the wall in places.

age and partly to the superimposed bacterial infection. They appeared sufficient to account for the general debility shown by some animals.

PROTOCOLS

C-270.—Male mongrel; weight 24 kilos. January 3, 1918, gassed 30 minutes with chlorine, 858 parts per million. Died three hours after exposure.

Autopsy.—Tracheal and bronchial mucosa opaque, necrotic looking, and easily peeled off. Lungs extremely edematous and congested.

Microscopic examination shows a severe diffuse injury to the lining epithelium of the air passages, large and small, and focal necrosis of the lungs, with practically no cellular inflammatory reaction. Sheets of hyaline necrotic epithelium are, in most places, loosely adherent as in Figure 49, but some bronchioles are plugged with fragments of detached membrane,

as shown in Figure 60. The general engorgement of the pulmonary capillaries is the outstanding feature of the lung changes. Relatively little precipitated edema fluid is seen in the alveoli. The sheaths of the large blood vessels, are, however, extremely edematous with prominent dilated lymph vessels. Numerous foci of necrosis are seen involving the atria and the adjacent alveolar septa. Figure 50 shows very well the size and relations of such an area. Special stains show a thick layer of fibrin along the dead alveolar walls.

Anatomical diagnosis.—Necrosis of tracheal and bronchial mucosa; focal necrosis of lungs; extreme congestion and moderate edema of lungs.

NOTE.—The short duration of life after gassing (less than three hours) accounts for the absence of appreciable cellular inflammatory reaction. The case illustrates well the early changes following chlorine injury.

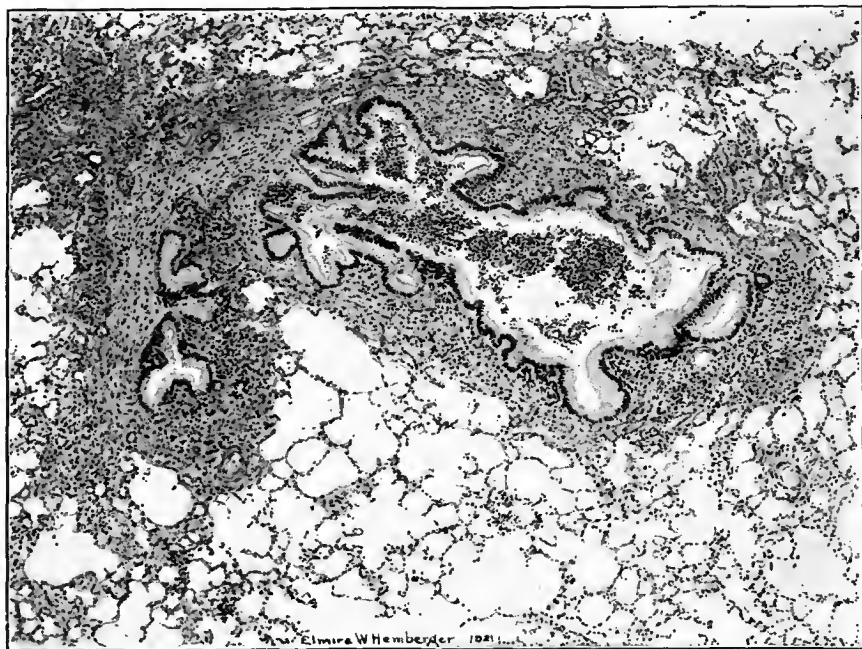


FIG. 58.—Chronic bronchitis and patchy emphysema in a dog dying 58 days after chlorine gassing

C-136.—Young male cocker spaniel. November 17, 1917, gassed 30 minutes with chlorine, 847 parts per million. Salivation and defecation during exposure, and evidence of marked respiratory irritation. Died eight hours after gassing.

Autopsy.—Apart from congestion of the abdominal organs, pathological changes are limited to the respiratory tract. The trachea and large bronchi show an opaque, grayish membranous lining in place of the normal velvety mucosa. The lungs are diffusely edematous, and deeply congested. There is also marked edema of the mediastinal tissues.

Microscopic examination shows complete necrosis and sloughing of the mucosa of the trachea and bronchi, with a widespread polynuclear reaction, and much edema of the entire wall. (Fig. 61.) The more superficial mucous glands are necrotic with an invasion of leucocytes. The injury and reaction in the smaller bronchi are equally well seen. The pulmonary capillaries are widely dilated throughout. There is very little albuminous precipitate or fibrin in the alveoli, and few free cells except in the atria and bronchioles. Here and there are typical foci of hyaline necrosis as shown in Figures 49 and 50.

Anatomical diagnosis.—Acute necrotizing tracheitis and bronchitis; edema, congestion and focal necrosis of lungs.

NOTE.—The findings are typical of acute chlorine poisoning. The inflammatory reaction was well advanced in the trachea and bronchi, although death occurred only eight hours after gassing.

C-134.—Male collie; weight, 16 kilos. November 16, 1917, gassed 30 minutes with chlorine, 867 parts per million. Died 24 hours after gassing.

Autopsy.—Lungs are voluminous, heavy, and deeply congested. In the trachea and bronchi there is a membranous exudate throughout and the walls of the air passages are quite edematous. No pneumonic patches are seen or felt.

Microscopic examination.—The most striking changes are found in the trachea and bronchi. The mucosa is necrotic and in most places sloughed off, leaving a denuded surface or only the basal layer of epithelium. (See Fig. 51.) The tracheal wall is infiltrated by leucocytes, with an outpouring of serum. The adventitia of the blood vessels is extremely edematous (see fig. 51), with widely dilated lymph channels, filled with precipitated lymph. In the alveoli there are, in addition to the edema, a few free cells. Some of these are polynuclears, others are desquamated epithelium. There are no frank pneumonic foci. Several small areas of focal necrosis of the septa are seen, with more or less hemorrhage.

Anatomical diagnosis.—Necrotizing tracheitis and bronchitis; focal necrosis and hemorrhages in lungs; pulmonary and mediastinal edema and congestion.

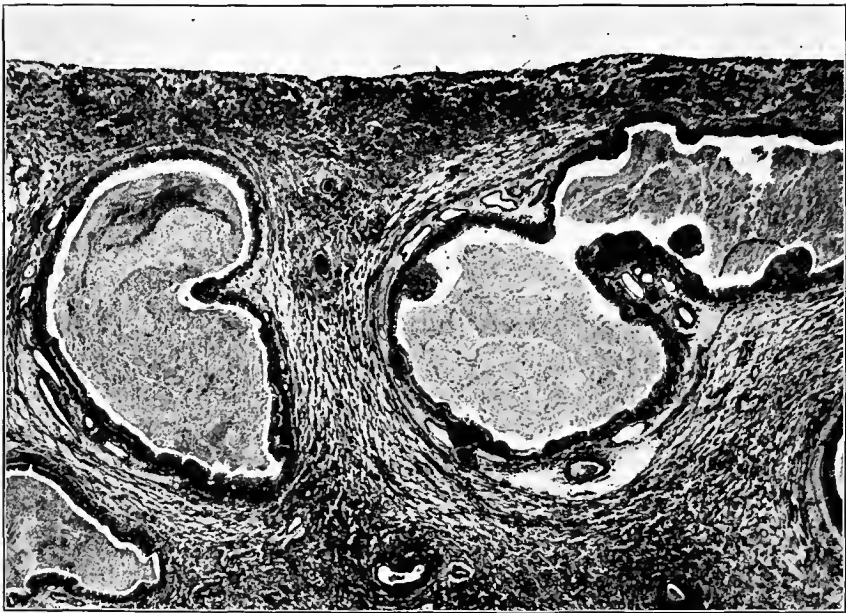


FIG. 59.—Bronchiecatic cavities in lungs of dog dying 39 days after chlorine gassing. The lung tissue supplied by these bronchi is completely atelectatic

NOTE.—In view of the widespread loss of the protective lining of the upper respiratory tract, with the evidence of tracheal infection, it is rather surprising that a bronchopneumonia had not developed. This would undoubtedly have occurred had the animal lived much longer. The early regenerative changes in the bronchial epithelium show the rapidity with which repair takes place.

C-109.—Brindle male mongrei; weight, 18.2 kilos. October 31, 1917, gassed with chlorine 30 minutes. Condition following gassing fair, but respiration became somewhat labored. Refused food and appeared depressed, but able to walk about. Condition remained about the same until death on November 5, five days after gassing.

Autopsy.—Body weight, 16.4 kilos, a loss of 1.8 kilos after gassing. The lungs are deeply congested, heavy, firm, and contain very little air.

Microscopic examination.—The lungs present an unusually complex microscopic picture, showing a confused mixture of inflammatory and reparative changes. In a majority of the

bronchi the ciliated surface epithelium is lost, but in many places the remaining basal cells have proliferated to form a thick layer the thickness of three or more cells. Mitotic figures are easily demonstrable. (Fig. 62.) Along with this reparative process, there is evidence of acute infection, with masses of polynuclear leucocytes in both the bronchial lumen and wall. It is noteworthy that occasional bronchi of moderate size are found showing a practically normal ciliated mucosa. The lung parenchyma shows much the same changes as the bronchi—active regeneration of alveolar epithelium, interstitial fibroblastic proliferation, particularly about the bronchioles, fibrinous and cellular alveolar exudate, miliary abscesses, and hemorrhages. Specific stain shows a thick layer of fibrin on the alveolar wall in many places. There is active proliferation of the surface cells of the pleura, with a prominent deeply staining layer.

Anatomical diagnosis.—Necrosis and regeneration of respiratory epithelium (tracheal bronchial, alveolar); suppurative and organizing bronchopneumonia.

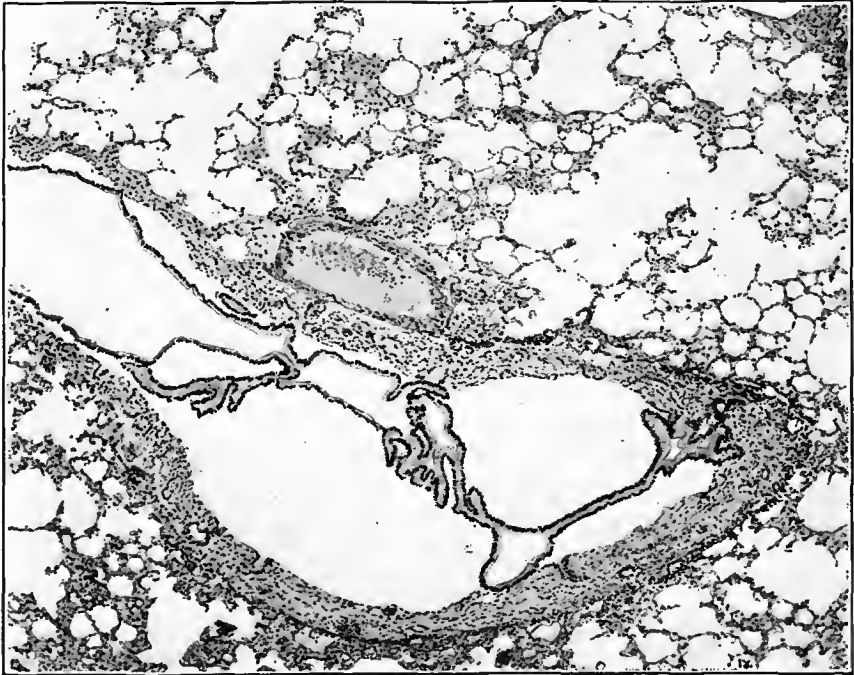


FIG. 60.—Sloughing of bronchial epithelium in dog killed three hours after exposure to chlorine

NOTE.—The case illustrates well some of the sequelæ of a moderately severe exposure to chlorine. The marked variation in the injury suffered by different bronchi is difficult to explain except on the assumption that the less-injured bronchi had been spasmodically contracted during exposure.

C-334.—Male setter; weight 10 kilos. January 17, 1918, gassed 30 minutes with chlorine, 716 parts per million. Recovered and sent to farm January 31, where he remained until May 14, approximately five months after gassing, when he was killed. Condition at this time was recorded as "somewhat emaciated and mangy."

Autopsy.—Pathological changes are limited to the lungs which are described as follows: The lower lobes are grayish pink and fairly well collapsed. The anterior margins of upper lobes are dark purple and airless, firm and nodular. Elsewhere in the upper lobes are light-colored emphysematous patches. On section the bronchi in both upper and lower lobes are conspicuous by reason of their thickened walls. In the upper lobes they are much dilated and filled with mucopurulent exudate. In the atelectatic areas along the anterior margins there is obviously a marked connective tissue overgrowth.



FIG. 61.—Acute necrotizing bronchitis 10 hours after chlorine gassing. There is complete sloughing of mucosa and a diffuse inflammatory reaction throughout the bronchial wall. Note the marked edema of tissue surrounding a large peribronchial vessel

Microscopic examination.—A number of sections from different portions of the lungs show very much the same pathological changes, namely, thickening and mononuclear infiltration of the bronchial walls, bronchiectasis, purulent bronchitis, patches of organizing pneumonia, focal obliterative bronchiolitis. (Figs. 63, 64, and 65.) Gram-positive diplococci are found in the bronchial exudate.

NOTE.—The widespread and advanced inflammatory changes in the bronchi and lungs are quite adequate to account for the poor condition of the animal when killed. Since the lesions were apparently progressing, the dog would no doubt have succumbed within a comparatively short time.

C-55.—Young male collie; weight, 14.4 kilos. September 28, 1917, gassed 30 minutes with chlorine, 678 parts per million. Stood gassing well and after a few days appeared to be in normal condition. Regassed on October 20, 22 days after first exposure, 30 minutes; concentration 710. Stood gassing poorly, and though the acute period was passed without

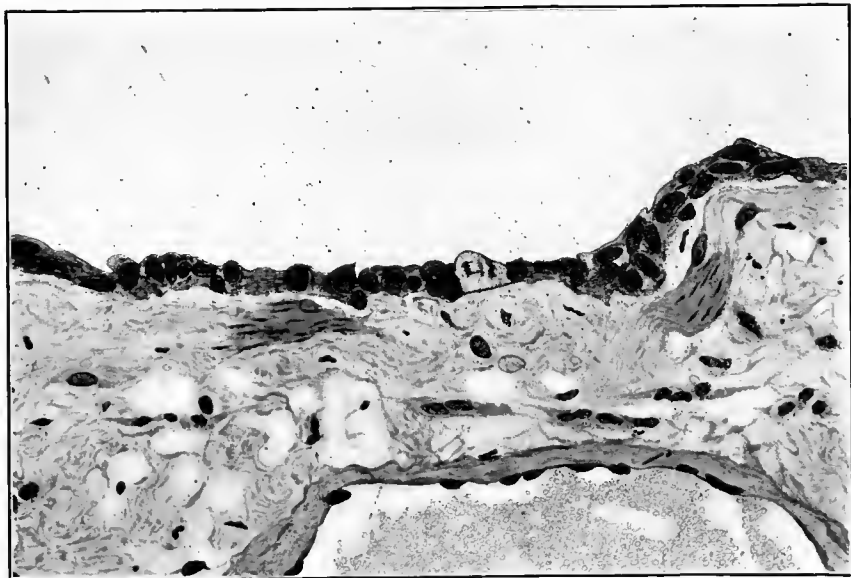


FIG. 62.—Regeneration of bronchial epithelium four days after chlorine gassing. One mitotic figure is seen

marked respiratory disturbance, a cough persisted. Killed with chloroform November 6, 39 days after first gassing and 17 days after second gassing.

Autopsy.—Body poorly nourished and anemic. Lungs are irregularly collapsed. The most outspoken changes are in the bronchi, many of which are greatly dilated and filled with pus. In other parts of the lung there are foci of obliterative bronchiolitis, with radiating scars, and more or less emphysema.

Anatomical diagnosis.—Chronic bronchitis and bronchiectasis; obliterative bronchiolitis; focal atelectasis and emphysema; anemia.

NOTE.—The case shows unusually advanced lesions involving primarily large and small bronchi. The changes were no doubt intensified by the second gassing, and would probably have ultimately caused the death of the animal from a flare-up of the persistent respiratory infection.

PHOSGENE

The mode of action of phosgene accounts for the localization and character of the chief anatomical changes resulting from its inhalation. The toxicity of the gas, as has been pointed out elsewhere, is due to the fact that in the pres-

ence of water it is split up into hydrochloric acid and carbon dioxide. When inhaled, little decomposition takes place until the gas reaches the lungs where, in the small air passages and sacs, it comes into contact with sufficient water vapor to bring about the evolution of hydrochloric acid. According to Hoover,⁴ much of the phosgene taken into the lungs is probably absorbed as such, decomposition taking place gradually in the tissues. This would explain the severe damage to the bronchiolar and alveolar epithelium, and would account for the more gradual development of the signs of pulmonary injury than is the case with certain other gases of the respiratory irritant group, such as chlorine and bromeyanogen, which do not require for their action any preliminary decomposition. It may be observed, in this connection, that although the phosgene injury is referable to the hydrochloric acid formed from it, the effects of phosgene and hydrochloric acid inhalations are by no means identical. On the contrary, the lesions produced by the two gases differ both in extent and degree. Hydrochloric acid injures most severely the larynx and trachea, damaging less the distal portion of the respiratory tract, while in the case of phosgene poisoning, it is the distal portion which is most affected. The

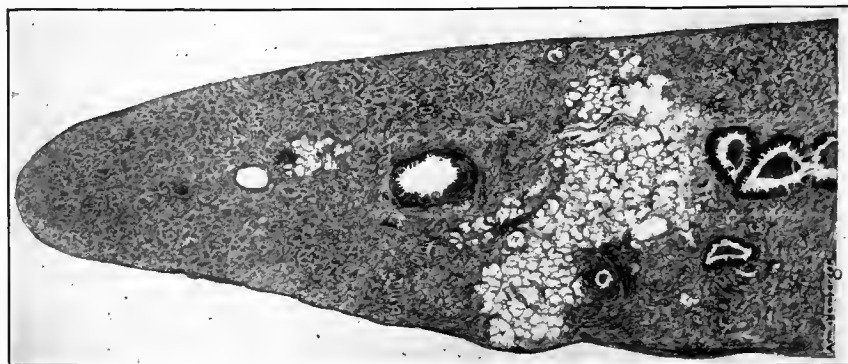


FIG. 63.—Low magnification of lung of dog dying two months after exposure to chlorine. Chronic bronchitis and bronchiectasis with atelectasis and occasional patches of emphysema

importance of the locus of decomposition is further emphasized by the observation that if animals are exposed to hydrochloric acid and phosgene in equivalent concentrations, the former is found to be distinctly less toxic, probably because its action is expended on the less vital proximal portion of the respiratory apparatus.

Extensive and detailed studies of the pathological changes induced by phosgene on experimental animals have been made both in this country and in England, but since the chief purpose of this chapter is to review the work done in America, the studies carried on by the medical section of the Chemical Warfare Service will be presented in some detail, with a brief review of the findings of British workers.

Investigations were conducted at both American University, Washington, D. C., and Yale University, New Haven, Conn. At the former station, a comparative study of the lesions in various animals was made, while at New Haven a systematic study of the changes in dogs, from the earliest to the most chronic lesions, was made, using animals gassed in connection with the studies upon the mode of action of phosgene and the treatment of the condition produced by toxic inhalations of the gas.⁵

The dogs were exposed in closed chambers for 30 minutes to concentrations varying from 44 to 120 parts per million. Although with higher concentrations there was, as has been pointed out in Chapter X, a more rapid onset of symptoms and a larger percentage of fatalities, the changes in the respiratory tract, as far as it has been possible to determine, were practically the same with high and low concentrations, except in respect to the time required for the development of the lesions.

AUTOPSY FINDINGS

The animals dying after gassing were autopsied, in most cases within a few hours. Dogs which did not succumb within two or three days (designated "recovered animals") were sent to a farm where a certain number died sooner or later (Table 51). The remainder of the recovered dogs were killed at intervals up to 129 days after gassing, and complete autopsies were performed.

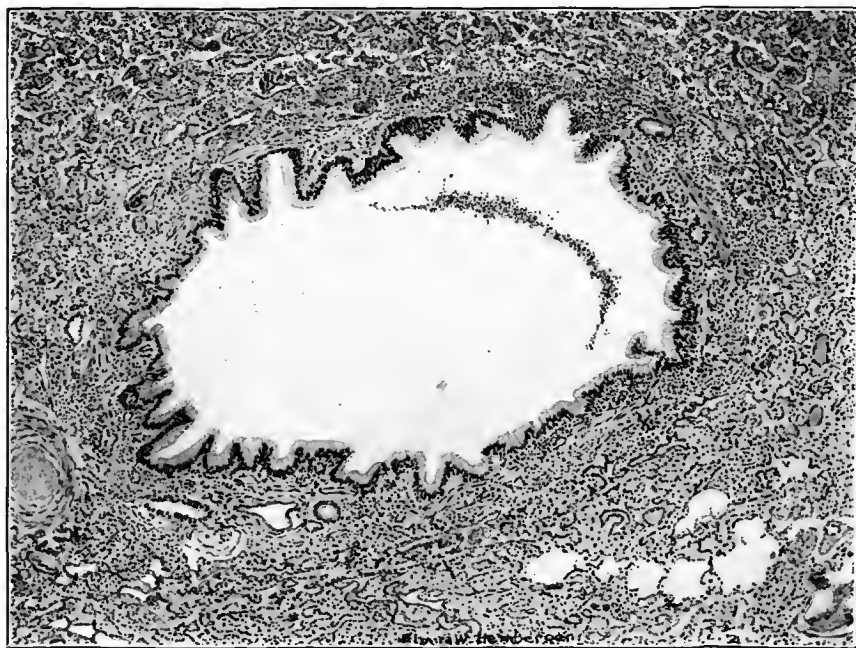


FIG. 64.—Higher magnification of the bronchi shown in Figure 63. Bronchus is moderately dilated. Adjacent lung tissue is atelectatic

In order to study the very earliest changes, a few animals were killed shortly after gassing, before the development of marked symptoms.

As might be expected, the changes found at autopsy, after fatal gassing, varied with the length of time the animal had survived. For this reason it will make for clearness of description if the findings in the several stages, which may be conveniently termed "acute," "subacute," and "chronic," are discussed separately.

These periods are arbitrarily divided as follows: (1) Acute, death within 48 hours; (2) subacute, death 3 to 10 days; (3) chronic, survival of 10 days or more. The accompanying table shows the number of animals falling into each of these groups and, in addition, the deaths by days up to the fifteenth day. Omitting the "killed animals," it is seen that in the majority of cases death occurred within the first 24 hours, and that the number of deaths in

each successive 24-hour period diminished progressively until the tenth day, when the base line was nearly reached (Chart XXV). It should be clearly stated, however, that the figures given in the table, and the curve based on them, refer only to autopsied animals, and do not include all of the dogs from any single experiment or series of experiments. In other words, the figures are intended to show only in a rough way the time at which death is likely to occur after phosgene gassing.

ACUTE DEATHS

Out of 503 animals gassed 376 died, of which 256, or 68 per cent died within the first 48 hours. Analyzing the figures further, we find that most of the deaths (195 of the 256) took place between 12 and 24 hours after gassing,

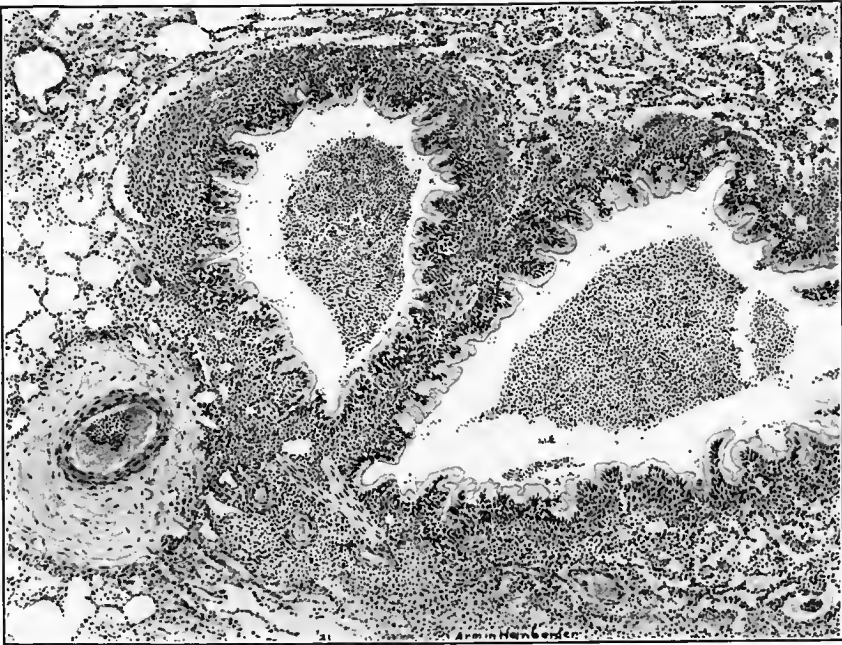


FIG. 65.—Higher magnification of two bronchi shown in Figure 63. Lumina are filled with a cellular inflammatory exudate. There is also a chronic peribronchial reaction

there being only 29 in the first 12 hours, and 32 between 24 and 48 hours. In other words, the critical period, as Underhill and others have shown, lay in the second 12 hours after gassing.

TABLE 51.—*Dogs gassed with phosgene*

Time of death after gassing	Total cases	Died	Killed	Time of death after gassing	Total cases	Died	Killed
Group I:				Group III:			
1 to 12 hours	29	29	0	Eleventh day	0	0	0
12 to 24 hours	197	195	2	Twelfth day	5	3	2
Second day	34	32	2	Thirteenth day	4	3	1
Group II:				Fourteenth day	3	3	0
Third day	23	20	3	Fifteenth day	2	0	2
Fourth day	16	11	5	Sixteenth to one hundred and twenty-ninth day	163	60	103
Fifth day	8	8	0				
Sixth day	7	4	3				
Seventh day	3	2	1				
Eighth	3	3	0				
Ninth day	1	1	0		503	376	127
Tenth day	5	2	3				

TABLE 52.—*Dogs gassed with phosgene*

Animals dying—	Died	Killed	Total cases
Group I. First 48 hours	256	4	260
Group II. Third to tenth day	51	15	66
Group III. Eleventh to one hundred and twenty-ninth day	69	108	177
	376	127	503

The gross anatomical changes found in animals dying acutely, though very striking, showed little variation. After the first, second, or third autopsy, the impression was one of uninteresting sameness, relieved only by the remarkably severe and brilliant changes in the respiratory system.

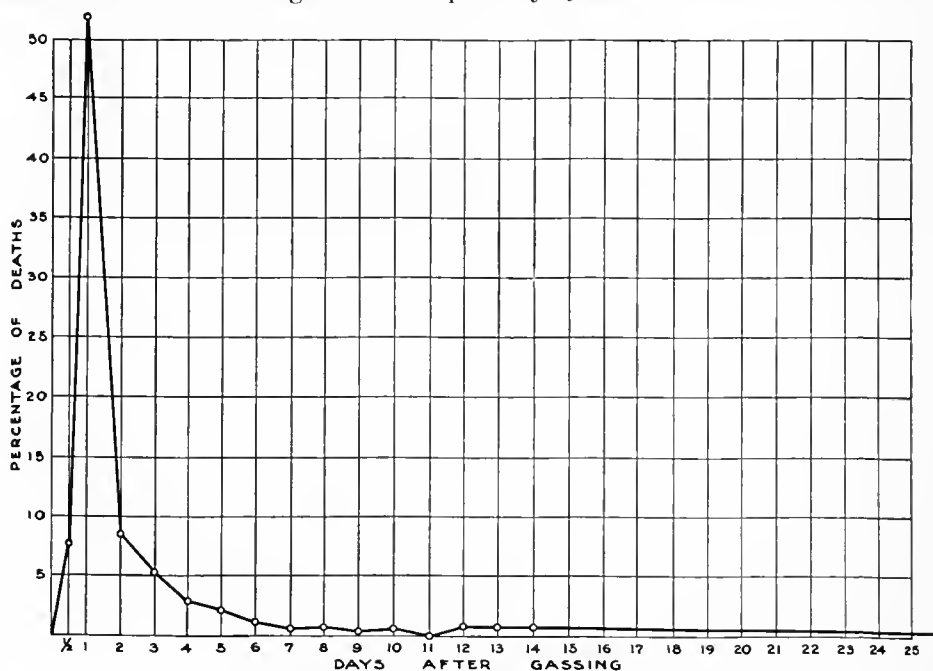


CHART XXV.—Duration of life after phosgene gassing

Frothy fluid, generally clear, but occasionally blood-tinged, oozed from the mouth. The conjunctivæ might be slightly reddened, but a frank conjunctivitis was rarely seen. Decomposition proceeded rapidly after death, as in chlorine poisoning, and was quite marked if the autopsy was delayed more than three or four hours, unless the body was kept chilled. The body weight was regularly less than at the time of gassing. This difference was often considerable, as the appended protocols show, amounting in the case of a large dog to as much as 1.5 kilos. The loss was probably due, in large part at least, to the escape of fluid from the edematous lungs through the mouth.

The engorgement of the great vessels and the congestion of the abdominal viscera were quite pronounced. The liver was swollen and extended well below the costal margin. Its dark purplish color was partly lost as the vessels were cut, allowing the blood to drain out. The spleen was only slightly enlarged but, like the liver and other abdominal organs, it presented the picture of acute congestion.

As the sternum was removed the voluminousness and noncollapsibility of the lungs were at once evident. The anterior margins nearly met in the median line and tended to overlay the heart. The pleural cavities were obliterated and it was unusual to find more than a few cubic centimeters of fluid in either the pleural or pericardial cavities. The loose tissue of the anterior mediastinum, however, as well as the interlobar pulmonary septa, were generally more or less edematous. The heart, as a rule, was quite distended. The distention was generally more pronounced on the right side. (Pl. XI.) In one animal that succumbed seven hours after exposure and was autopsied immediately, the apex of the heart was bifid by reason of the marked right-sided dilatation.^e The cavities and valves of the heart presented nothing abnormal except for the presence of flame-like hemorrhages beneath the endocardium, which were encountered not infrequently. They were found in approximately 15 per cent of the acute deaths. The commonest location of the hemorrhages was in the region of the papillary muscles of the left ventricle.

GROSS FINDINGS

Respiratory tract.—The larynx might be slightly edematous, but was otherwise normal looking. The trachea and bronchi were filled, more or less completely, with frothy fluid. The fluid was generally clear, faint yellow, and of the consistence of blood serum. In the small bronchi it might be slightly viscid, or even tenacious, owing to an admixture of mucus and fibrin. Hill ⁶ has pointed out that if the fluid is collected it may often coagulate on standing, but this phenomenon was not observed. The mucosa of the trachea and larger bronchi was usually of normal smoothness and color, except that between the cartilaginous rings it was at times slightly reddened from injection of its vessels, which presented, on close inspection, a fine network. The congestion was more marked in the smaller than in the larger bronchi.

The lungs were strikingly voluminous and quite heavy. The pleura was smooth, glistening, and moist, and its lymphatics were often distinctly dilated. In this early period a fibrinous or purulent exudate on the surface was practically never seen. The lungs were extraordinarily mottled; large whitish patches alternating with deep red ones. Over the whole, there was often a bluish cyanotic hue. The light-colored bodies were more or less elevated and crepitant, and were easily recognized as areas of acute emphysema. By reason of the distension, the individual alveoli could often be made out with the naked eye, and could be seen with great clearness by aid of a low-power magnifying glass. The darker portions of the lung appeared collapsed by way of contrast, but examination showed that these areas were not particularly atelectatic, but only less distended than the remainder of the lung tissue. The dark color was referable to the extreme congestion. The proportion of light-colored emphysematous lung tissue and dark congested, partially collapsed lung varied considerably. In some cases almost the entire lung was dark bluish red, with only a few scattered light patches in the upper lobes. In other cases, where the duration of life after gassing was the same, a widespread emphysema, with little of the dark red tissue, was found. In general the lower lobes were darker, the emphysema being more pronounced in the upper and middle portions.

^e The phenomenon of cardiac dilatation in gassed animals is discussed in some detail in subsequent pages.

On palpation the lung was doughy and pitted on pressure. Much fluid could be expressed through the bronchi. In animals dying in the first twelve hours, the edema was generally considerably less than in those living longer. In the latter, it was generally the most conspicuous feature, quite overshadowing the congestion and emphysema. In extreme cases, the rounded margins of the lung were quite translucent and the dark bluish-red color of the early period was transformed into a watery pink, as though even the stagnant blood in the vessels had become diluted.

In estimating the extent of the edema, the weight of the lungs, as has been pointed out in connection with chlorine gassing might be taken as a fair index, although it was evident that the greatly increased weight of the organ was due not to the edema alone, but in considerable part to the extreme congestion which was regularly present. Indeed, in the first few hours before the edema became well developed, the excess of blood was clearly responsible for the larger share of the increase in weight. Both the heart-lung and body-lung ratios were used as indices of edema. The former was suggested by Barcroft, and has been used by English observers. The normal indices were determined from autopsies on 15 normal dogs, and an average lung-heart ratio of 1.3 and lung-body-ratio of 0.0115 being found. Dividing the index obtained in the gassed animals by these normal ratios, a figure was obtained which probably represented fairly accurately the degree of edema present. Of the two indices, that based on the lung-body ratio was regarded as the more accurate in the average, medium-weight, well-nourished dog, but in small animals it often gave readings which were obviously too high. An objection to the lung-heart proportion is that even slight variations in the method of trimming the heart will lead to relatively large errors. Using the two methods, it was found that the lung increased rapidly in weight after gassing, reaching a maximum after about 24 hours, when it might be, in fatal cases, more than four times the normal. (For detailed figures see Table 53, Chart XXVI).

TABLE 53.—*Degree of increase in lung weight after gassing*

	Number of cases averaged	Increase based on—			Number of cases averaged	Increase based on—	
		Lung-heart ratio	Lung-body ratio			Lung-heart ratio	Lung-body ratio
Animals died:				Animals died—Continued.			
First 12 hours.....	10	2.32	2.53	Eleventh to one hundred and fourth day..	21	1.23	2.51
12 to 24 hours.....	65	2.50	2.84	Animals killed:			
Second day.....	13	2.50	2.74	Fifth to tenth day.....	4	1.47	-----
Third day.....	10	1.24	3.31	Eleventh to one hundred and fourth day..	25	1.13	1.20
Fourth day.....	6	1.36	3.32				
Fifth to tenth day.....	7	1.20	2.92				

¹ These figures do not indicate the degree of edema present, since practically all of the animals dying at this period had pneumonia. The cellular exudate in the lungs would account for the larger share of the increased weight of the organ.

While the cut surface of the lung was generally smooth and moist, close inspection might show tiny gray foci of bronchopneumonia. These were often overlooked in the gross specimen, being masked by the edema and congestion. The smaller bronchi were somewhat more conspicuous than normal owing to the edema of their walls.

Grossly, the blood vessels were quite normal looking. No thrombi were found in veins or arteries. Bronchial lymph nodes were somewhat enlarged and on section were distinctly edematous.



HEART AND LUNGS OF DOG DYING TWENTY-FOUR HOURS AFTER
PHOSGENE GASSING.

Light-colored patches of emphysema alternate with deep red congested and partially collapsed areas in the voluminous lung. Heart is dilated, particularly the right side.

Outside the respiratory system no pathological changes of any significance were found, other than the congestion of the abdominal viscera, and apparent dilatation of the heart already mentioned. In the stomach and intestines congested areas and hemorrhagic erosions were occasionally seen, but since similar lesions were not infrequently encountered in nongassed dogs, they were considered in no way related to gassing.

In 15 dogs the brain was examined, but in none could there be demonstrated capillary hemorrhages or inflammatory lesions such as were described by Mott ⁷ in human cases.

Examination of the pancreas, adrenals, and thyroid was in all cases negative.

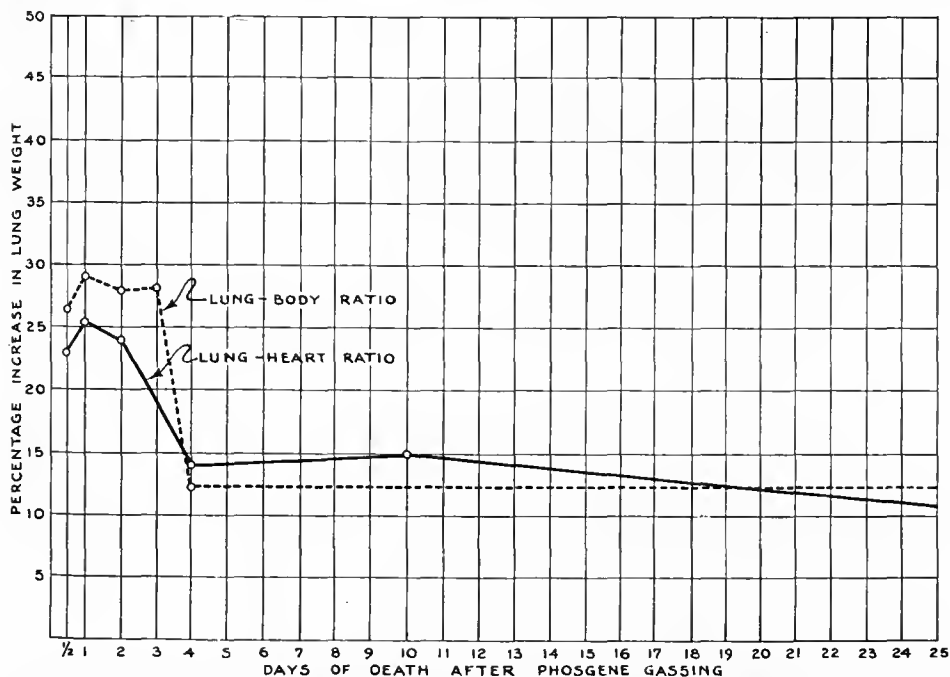


CHART XXVI.—Degree of pulmonary edema after phosgene gassing, as determined by lung-heart and lung-body ratios

MICROSCOPIC FINDINGS

Significant changes were found only in the lungs and smaller bronchi. The alveoli varied markedly in size, some being exceedingly large, with very thin, bloodless walls, while others showed partially collapsed walls containing greatly distended, tortuous capillaries. There might be considerable desquamation of the alveolar epithelium, particularly in the semicollapsed patches. The alveoli nearly everywhere contained more or less coagulated serum (edema), which might appear either as a homogeneous pink-staining material resembling thyroid colloid, or as a faint granular precipitate, the appearance depending apparently not so much on the quantity of fluid present as on its content.

In addition to serum there was generally some fibrin in the alveoli; occasionally this was quite abundant. But it was along the alveolar walls that

fibrin appeared in greatest amount. With special stains, a thick layer lining the alveolus could be demonstrated in many places, with frequent strands crossing the capillary to a similar layer on the wall of the adjacent alveolus. (Figs. 66 and 67.) It was evident that the presence of fibrin in this situation must not only interfere with gaseous exchange but, as will be emphasized in the discussion of the circulatory disturbances, also must constitute a serious obstacle to the flow of blood through the lungs. As in chlorine gassing, variations in the lumina of the cartilage-free bronchi were seen, which suggested alternate dilatations and constrictions, but one could not be certain that such pictures represented a condition that was not referable to post-mortem changes, such as irregular collapse of the lung. This point is discussed elsewhere (p. 457).

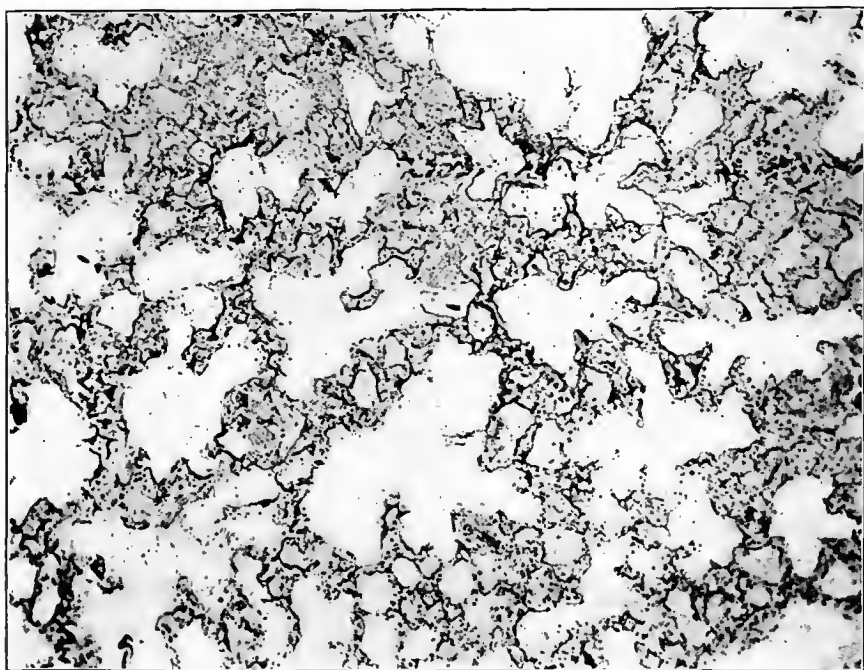


FIG. 66.—Lung of dog dying two days after exposure to phosgene. Fibrin stains show a heavy deposit along the alveolar walls, outlining them everywhere quite distinctly

The very large bronchi, like the trachea, showed little change, though there might be an excess of mucus and some polynuclear leucocytes in their lumina.

The epithelium was perfectly preserved, even the cilia being seen as distinctly as in the normal animal. The finer bronchial tubes, however, showed evidence of serious damage.

As early as two hours after exposure there was histological evidence of necrosis of the epithelium. The surface was covered by a thick layer of eosin-staining material made up of mucus and dead desquamated epithelium. Beneath this necrotic layer there might remain a thin layer of flattened or rounded basal cells. In some cases these basal cells were destroyed, the tube being lined by a pink-staining necrotic membrane.

The difference in the injury suffered by the proximal and distal portions of the respiratory tree was well shown by the use of vital stains. Ten dogs were injected intravenously on two successive days with 100 c. c. of 1 per cent solution of the dye, and then exposed for a half hour to a concentration of phosgene varying between 80 and 97 parts per million. One animal was killed after two hours, and others at varying intervals up to three days. Frozen sections, counterstained with carmine, were made from different portions of the respiratory tract.

In no instance was the tracheal epithelium vitally stained. The bronchial epithelium, on the other hand, was stained in places, and in the finer bronchioles the coloration was marked, affecting the entire wall quite uniformly. All

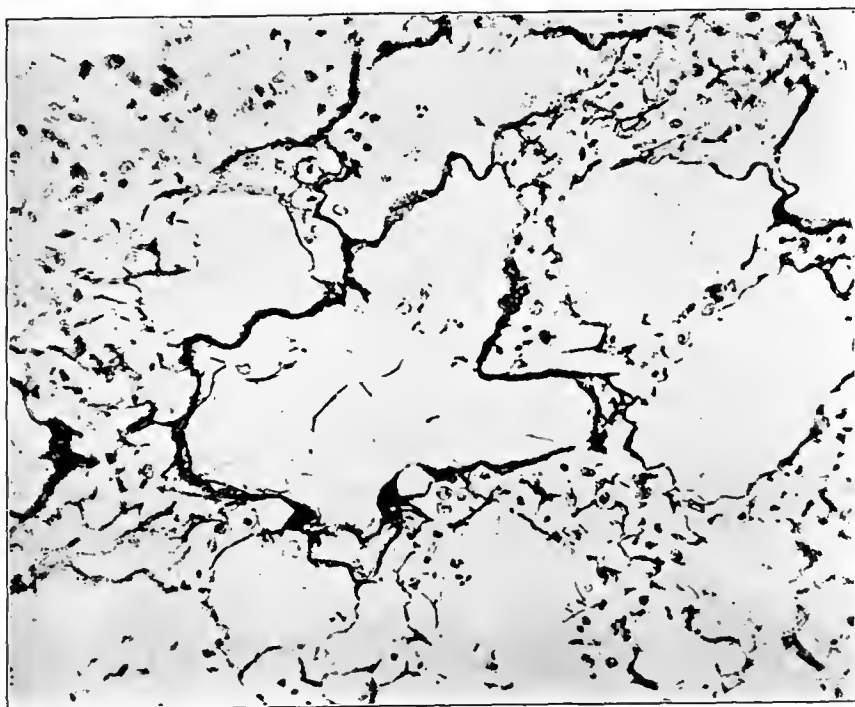


FIG. 67.—Higher magnification of an area shown in Figure 66. In places the fibrin stain extends across the septa

of the bronchioles, however, were not equally affected. Some showed unstained epithelium, whereas the lining cells of other bronchioles in the immediate vicinity were deeply colored. The staining seemed most marked where there was distortion of the tube with either contraction or dilatation. The flat alveolar epithelium seemed unaffected. These results were obtained in animals that were sacrificed as early as two hours after exposure.

In addition to the necrotizing effects just described there were often seen, even in early deaths, a beginning inflammatory reaction. The reaction was practically always focal at this stage, with its point of origin in a bronchiole. (Fig. 68.) There was evidence, however, of what may be considered a general inflammatory reaction in the lungs. Nearly everywhere there was an increase in the number of polynuclear leucocytes in the alveolar walls and occasionally

they were seen in process of migration into the alveoli and fibrin; sometimes a considerable amount might be found in the alveolar exudate. The extent of the focal pneumonic process varied in different animals. Many showed no reaction at all.

A tabulation of the cases studied shows (Table 54) that pneumonia was demonstrated in approximately 50 per cent of the animals dying in the first 48 hours.

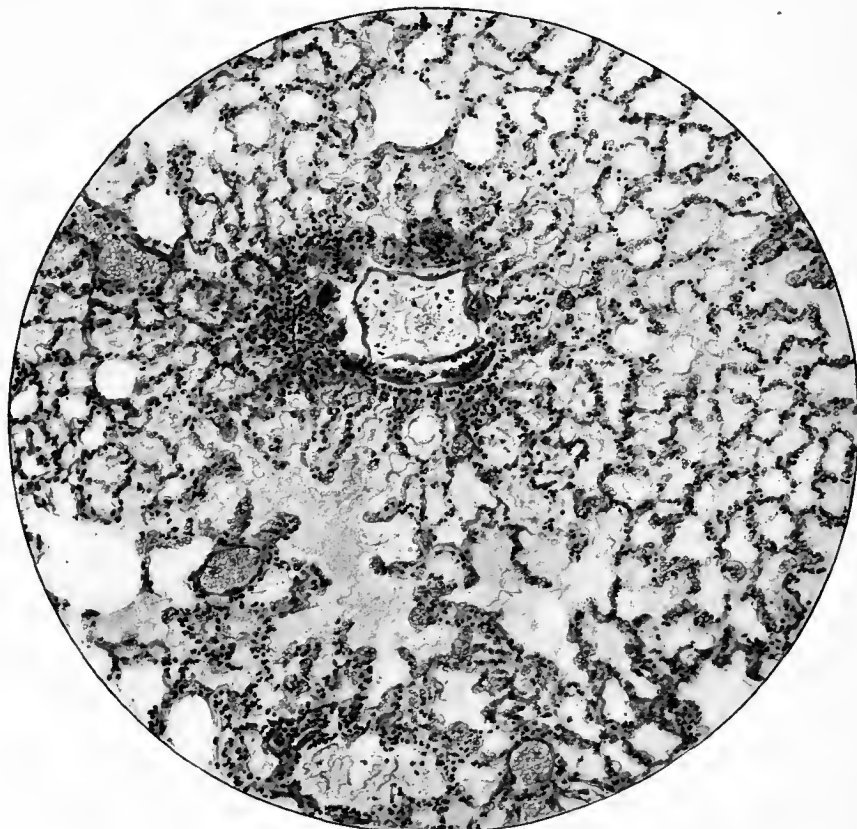


FIG. 68.—Early inflammatory reaction about bronchiole 18 hours after gassing. Cells are chiefly polynuclears. There is a generalized edema of the lung tissue

TABLE 54.—*Pulmonary complications in dogs gassed with phosgene*

	Pneumonia				Bronchitis			
	All types	Early	Ad- vanced	Organiz- ing	All types	Early	Ad- vanced.	Organiz- ing
Animals dying:	<i>Per cent.</i>	<i>Per cent.</i>	<i>Per cent.</i>	<i>Per cent.</i>	<i>Per cent.</i>	<i>Per cent.</i>	<i>Per cent.</i>	<i>Per cent.</i>
Group I. First 48 hours.....	48	48	0	0	59	57	2	0
Group II. Third to tenth day....	90	12	53	25	96	20	48	28
Group III. Eleventh to one hun- dred and twenty-ninth day.....	50	12	26	12	75	6	53	16
Animals killed:								
Group I. First 48 hours.....	50	40	10	0	50	40	10	0
Group II. Third to tenth day....	23	8	0	15	100	0	100	0
Group III. Eleventh to one hun- dred and twenty-ninth day.....	9	6	0	3	68	2	32	34

The content of the blood vessels in the lung appeared to be, in all cases, simple post-mortem clot, which, however, was strikingly rich in fibrin. (See fig. 67.) The question of the presence of fibrin thrombi in the capillaries described by Klotz¹ and others is discussed elsewhere. The extension of fibrin masses through the alveolar walls and capillaries and its importance has been referred to already.

The adventitia of the larger vessels was spread apart by edematous fluid, as in chlorine poisoning. (See fig. 53.)

The bronchial lymph glands showed a dilatation of their peripheral sinusoids, which contained mononuclear cells, red blood cells and occasional polynuclear leucocytes. The channels through the glands were often spread apart much more widely than usual and showed a similar cell content.

In the liver the hepatic veins were everywhere distended, and the engorgement was noticeable also in the capillaries which directly joined these vessels. In this central zone the liver cells were thinned out as though compressed, giving the typical picture of passive congestion as seen in man. There was generally no necrosis of the liver cells and no inflammatory reaction. In a few cases focal areas of necrosis were found, but on account of the rarity of this lesion we have considered it accidental and not related to the gassing. In the same way we have interpreted a single instance of hemorrhagic cystitis and renal epithelial necrosis.

SUMMARY OF CHANGES

The important acute changes brought about by exposure to lethal concentration of phosgene gas were confined to the cardiorespiratory system. The upper respiratory tract was unaffected, and this was in marked contrast to the changes in the lungs and finer bronchi.

The lungs were the seat of an intense edema and congestion which was associated in many cases with focal inflammatory changes originating in the bronchioles. The inflammatory exudate was not confined to the bronchioles, but spread to a variable extent into the surrounding alveoli, so that a picture of early bronchopneumonia was found superimposed upon intense edema of the lung. Plugging of the bronchioles with exudate was associated with areas of partial atelectasis and emphysema of the lung tissue. The presence of an abundance of fibrin on and in the alveolar walls, crossing and obstructing the capillaries everywhere, offered an explanation for the increased resistance in the pulmonary circulation and the consequent dilatation of the right side of the heart.

SUBACUTE STAGE: DELAYED DEATHS

There were, altogether, 66 dogs in this class, 15 of which were killed, and 51 died 3 to 10 days after gassing. The pathological picture, both gross and microscopic, was more varied at this period than in the earlier and more acute stage, where, as we pointed out, there was a certain uniformity, especially in the gross characteristics. On account of this variation, it will be necessary, in describing the findings, to subdivide the cases further into at least two classes: (1) Those that died; (2) those that were killed.

In the animals that died the anatomical changes were characterized by the presence of a severe and widespread inflammatory process in the respiratory tract. Thus Table 54 shows that in 90 per cent pneumonia was found at autopsy and bronchitis in 96 per cent.

GROSS FINDINGS

The general appearance of the body, abdominal organs, and heart was practically the same as in the acute deaths. The chief differences were found in the lungs, which, in addition to edema, congestion, and patchy emphysema, showed quite regularly a more or less widespread inflammatory process, affecting both the smaller air passages and air sacs.

Grossly, the lungs were very voluminous and heavy. The surface was generally smooth and uniform, but very frequently firm, pale pinkish areas, often irregularly wedge-shaped, stood out in sharp contrast to the remaining portion of the lung, which was cushiony and crepitant. In animals that survived only three days, these solid areas were not as conspicuous as in the animals that lived longer. In practically all cases the consolidation was more extensive in the thinner lappets and near the margins of the lung. The posterior and dependent portions of the lung might be involved in the pneumonic process but, as a rule, parts which in the early deaths showed the greatest edema were not so regularly consolidated. It may be recalled in this connection, as previously noted, that the upper lobes are the more dependent in dogs and other four-footed animals.

Perivascular edema, as in the acute stage, made the larger vessels of the hilus conspicuous. In the vessels only post-mortem clots were found; no thrombi were present.

On section the lungs varied in their appearance according to the length of survival of the animal. In the more acute deaths the lungs were still very wet, and it was sometimes difficult to make out the areas of consolidation which later stood out as dry granular areas that varied in size from a few millimeters to many centimeters. The dry granular areas were dark and reddish-brown in color, not nearly as translucent as the areas of edema and congestion, and very much firmer. In the smaller areas of consolidation there was almost always a central bronchiole on account of its thickened wall and the purulent exudate in its lumen. In animals surviving longer the areas of consolidation stood out much more strikingly and might involve the greater portion of a lobe, although as a rule only one-third to one-half of the lobe was affected. Not infrequently three or more lobes would contain extensively hepatized areas. The consolidation was generally pseudo-lobar in type but small discrete patches of bronchopneumonia might be seen scattered through the less affected lobes.

MICROSCOPIC FINDINGS

Histological studies corroborated the gross findings. With the exception of a few subsidiary lesions in the other organs, the changes were found only in the respiratory tract.

In all instances, the bronchioles were much altered. They were more or less dilated and appeared as large, round holes, filled with exudate, consisting of cellular debris, leucocytes, and red blood cells. In many places the lining epithelium was entirely lost and the walls were structureless. About such bronchioles there was generally an active pneumonic process, sometimes quite extensive and merging into other similar foci. In such areas, the alveolar walls might be necrotic, with the development of frank abscesses. The inflammatory exudate was often quite hemorrhagic. (Fig. 69.)

The pneumonic zone faded rather abruptly into areas where the lung tissue was well preserved. The alveoli here, as in the more acute stage, might be partially collapsed or emphysematous. Their walls were always prominent on account of the dilatation of the vessels and the partial desquamation of the alveolar epithelium. The alveoli in this zone contained some fibrin and serum with occasional desquamated cells and leucocytes. That this was a very early inflammatory process was evident from the large number of polynuclear leucocytes caught in process of migration from the vessels.

The pneumonia was often widespread, approaching a lobar distribution, but it was fairly clear that the infection in these cases, as in the more patchy pneumonias, was bronchial in origin. Organization of the exudate was seen now and then, but was a much more common finding in the "recovered" dogs that were killed, as will be described later.

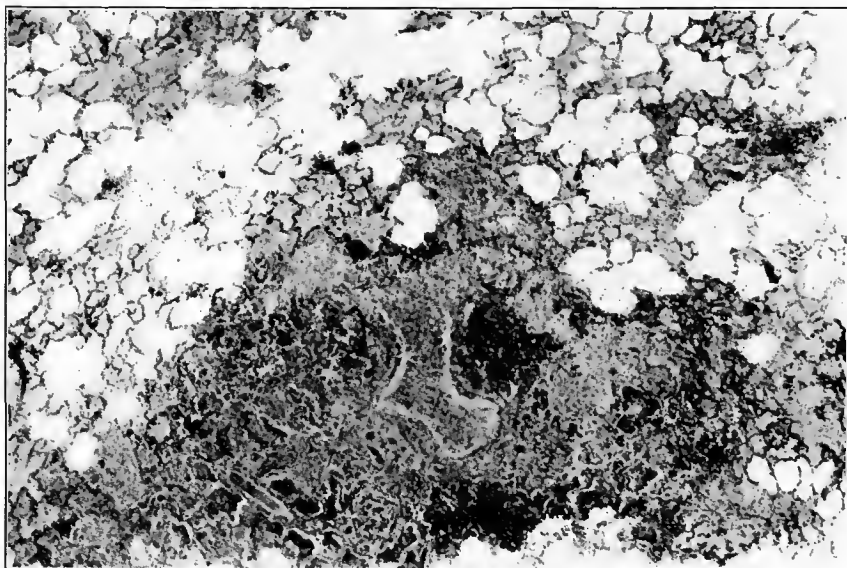


FIG. 69.—Bronchopneumonia causing death seven days after exposure to phosgene. The bronchial wall is necrotic and there is considerable hemorrhage in the pneumonic exudate. Lung is moderately edematous.

The bacteriology of these pneumonias was investigated in 23 cases, with the following results: *Streptococcus hemolyticus* was found alone in 10 cases; *Staphylococcus aureus* alone in 6 cases; *Streptococcus* and *Staphylococcus* together in 3 cases; *Streptococcus* and other organisms once in 2 cases; miscellaneous or undetermined organisms in 2 cases.

It is seen that a hemolytic streptococcus was the most common organism met with, being demonstrated in 13 out of 23 cases. It was not possible to show a relationship between the type of organism present and the character of the pneumonia, although the impression was obtained that abscess formation and organization were more often associated with the staphylococcus than with other organisms. It may be of interest to note that in a few cases of pneumonia among nongassed dogs, autopsied about the same time, the bacteriological findings were roughly the same as in the gassed animals.

Microscopic findings, outside the respiratory system, were of little interest. In the liver the changes were very similar to those described in acute deaths. The congestion in the hepatic vein persisted and frequently the liver cells in the immediate vicinity were reduced to fine strands, with the intervening sinusoids greatly congested. These liver cells contained brown pigment, but very rarely was there any nuclear disintegration or leucocytic infiltration. The kidneys showed cloudy swelling of the tubular epithelium and occasionally the glomeruli would be markedly congested, but there was no evidence of any serious or permanent damage to the renal parenchyma.

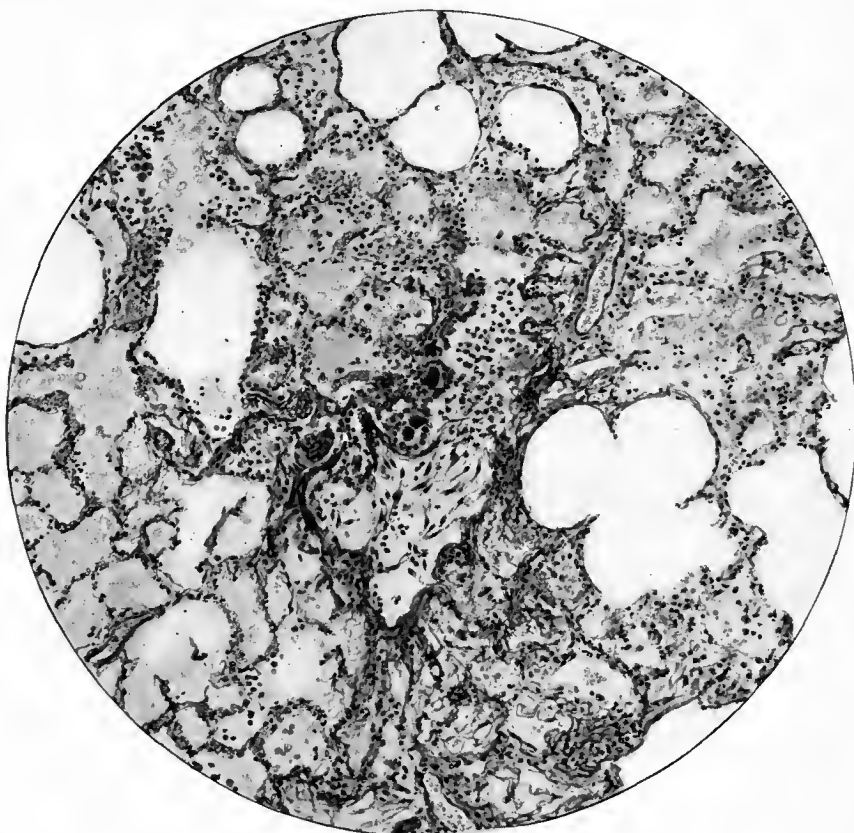


FIG. 70.—Early stage of organization of pulmonary exudate four days after phosgene gassing

KILLED DOGS

Fifteen dogs that were apparently recovering from the gassing were killed from the third to the tenth day for a study of the reparative processes in the damaged lung. Although the majority of the animals showed no symptoms at the time they were killed, the respiratory tract in all cases presented the obvious effects of the gassing. In most cases congestion, edema, and emphysema were still present in a moderate degree, being quite marked in some, though rarely so extreme as in the early fatal cases.

The most striking gross feature of the lungs was the presence of small nodules which were scattered quite uniformly throughout the organ. To the

palpating finger they felt very much like tubercles, though not quite so firm and shotty. They were more readily palpated and could be seen easily as small gray semitranslucent foci, closely simulating miliary tubercles. A bronchiole could be identified sometimes in the center of the nodule. From the third to the fifth or sixth day, the nodules were not so sharply outlined nor so translucent and firm as they became later. Not infrequently they were made prominent by the presence of hemorrhages in their substance, the color being thus changed from gray to bright red.

The microscopic picture in most of the cases was much the same; a widespread organizing bronchitis and bronchiolitis. (Figs. 70 and 71.) Under

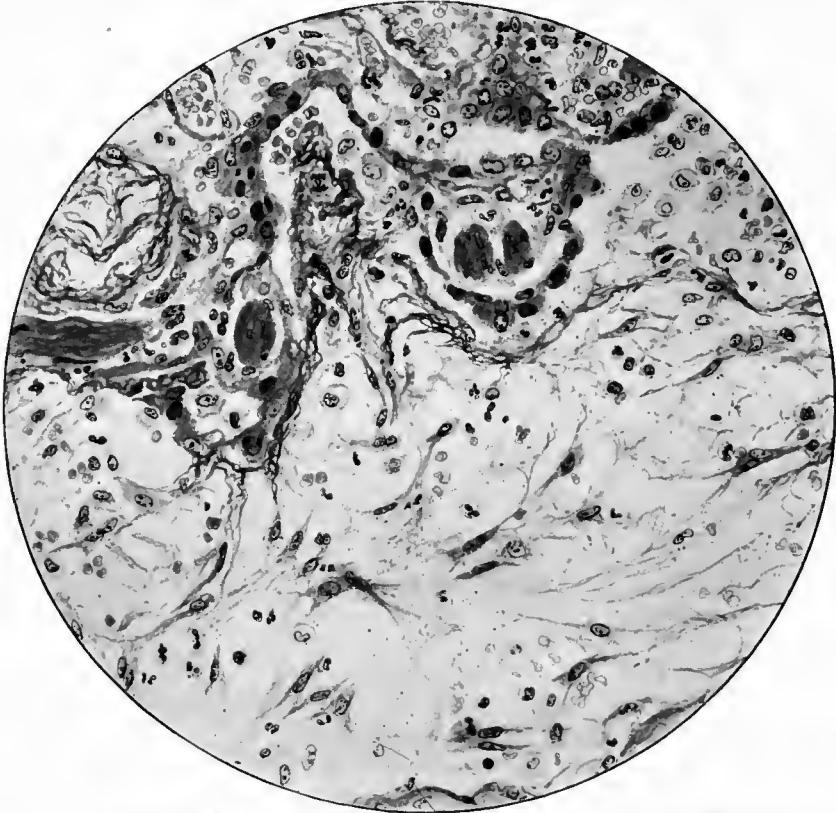


FIG. 71.—Higher magnification of bronchial wall shown in Figure 70. Fibroblasts are seen extending in a loose growth from the submucosa. One mitotic figure is present

very low magnification one could see a patch of cellular tissue about almost every bronchus, especially the smaller (the tubercle-like nodules seen in the gross). The tissue was composed of young fibroblasts, a few capillaries, and many mononuclear wandering cells. In quite a number of the bronchi there was an exudate which was undergoing organization, with permanent obliteration of the lumen. Fibrin stains showed that there was often considerable old fibrin in the midst of the organizing areas.

Polynuclear leucocytes and fresh fibrin were not present in any quantity in the typical cases, which suggested that the infection (bronchitis or early bronchopneumonia of the first stage) to which these lesions undoubtedly were the sequel, had been successfully combated.

SUMMARY

When death was delayed 3 to 10 days after exposure to phosgene, infection of the respiratory tract was the cardinal change found. The upper air passages remained practically unaffected except for a mild congestion, but there was intense necrotizing infection of the bronchioles which not infrequently involved the surrounding alveoli and resulted in the formation of miliary abscesses. These were surrounded by small zones of hemorrhagic pneumonia. The intervening lung tissue showed alveoli filled with varying amounts of serum, fibrin and cells. If death was delayed more than four days, beginning organization of the exudate in the alveoli and bronchi was generally seen.

Animals which have apparently recovered from acute symptoms of gassing and which showed no signs of pneumonia, when killed 3 to 10 days after gassing, showed a widespread organizing bronchiolitis which clearly represented the sequel of the acute bronchial and peribronchial inflammatory reaction, so prominent in the acute period.

CHRONIC STAGE: RECOVERED ANIMALS

There were 177 dogs which survived gassing more than 10 days. Of these, 69 died and 108 were killed between the eleventh and one hundred and twenty-ninth day. Description will be made easier and clearer if the "died" and "killed" dogs are considered separately. It may be pointed out, however, that some of the animals that were killed looked sick and in poor condition and would have died in a few days had they been left alone. As might be expected, the lesions found in such animals are practically the same as in those that died.

The pathological findings in the dogs that died differed little from those observed in the 5 to 10 day animals already described. The essential and dominating feature in a majority of the cases was an infection of the respiratory tract. Reference to Table 54 shows that in 50 per cent of the cases pneumonia of one type or another was present, and bronchitis in 75 per cent. It can be stated safely that death was referable to respiratory infection, acute or chronic in at least 65 per cent.

What, may be asked, was the cause of death in the remaining 35 per cent? In a few cases there was a chronic nephritis of the type not infrequently met with in dogs which may have been responsible. In the other 20 to 25 per cent no cause of death was found. These animals were all poorly nourished and anemic. In other words, lesions sufficient to account for death in at least 20 per cent of these animals were not demonstrated. It is possible, of course, that a careful study of the blood-forming organs or endocrine glands, not investigated in any of our cases, might have thrown some light on the question.

KILLED DOGS

A majority of these were well nourished and healthy looking. Some were thin and sluggish, and a few were in bad shape and obviously about to die. The findings in these sick dogs have been referred to in the previous paragraph.

The gross changes in the healthy looking animals were not very striking. Outside the lungs, there was little worthy of note. The trachea and larger bronchi were quite normal.

The lungs were moderately collapsed, but the collapse was not uniform. Plate XII illustrates very well the picture often seen. There were dark pink atelectatic patches here and there; the rest of the lung tissue was more or less emphysematous. Tiny, firm nodules might be felt or seen on section, but these were not at all conspicuous. The bronchi were more prominent than normal. Their walls looked thickened and in the lumina there was an excess of mucus.

Microscopically, the picture was somewhat more varied. The emphysema and atelectasis were more pronounced than the gross appearance would indicate.

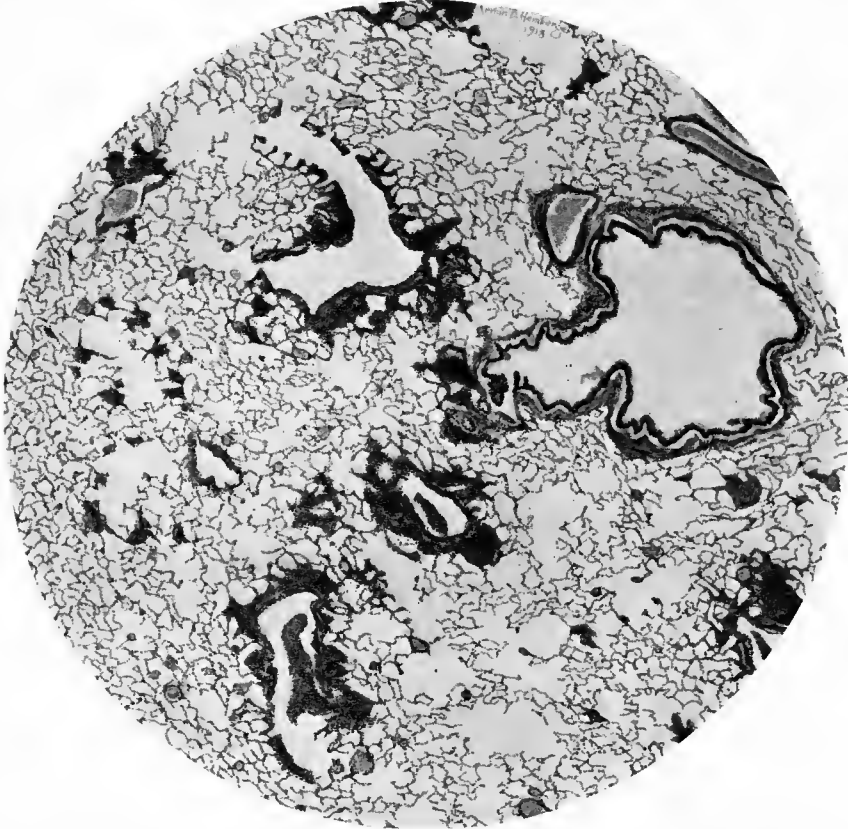


FIG. 72.—Organizing bronchiolitis in a dog killed 14 days after phosgene gassing. The lung grossly showed irregular patches of emphysema and atelectasis, and tuberclelike nodules were felt throughout the lung

The alveoli were not otherwise altered. The bronchi showed marked changes. There was a distinct fibrous thickening of the walls of some of the medium-sized bronchi, and an infiltration by mononuclear wandering cells, most marked in the outer coat. In a much larger number of cases the only change found was in the small-sized bronchi. Here the lumen in places was completely occluded by a mass of granulation tissue with a zone similar to newly formed cellular connective tissue immediately about the bronchus. (Figs. 72 and 73.) This lesion, which was a perfect example of obliterative bronchiolitis, clearly represented a more advanced stage of the organizing bronchiolitis and pneumonia found in the dogs killed three to ten days after gassing. These changes

in the bronchi were quite sufficient to account for the persistence of the atelectasis and emphysema, which was seen to be directly proportional to the extent of the bronchial lesions. The susceptibility of these chronic dogs to pneumonia was also probably referable to the presence of such foci of infection in the bronchial wall. (See discussion of residual pulmonary lesions, p. 508.)

PHOSGENE POISONING IN OTHER ANIMALS

A comparative study was made in the American University laboratories of the effects of phosgene on various laboratory animals, including monkeys, guinea pigs, rats, rabbits, mice, dogs, and goats. It was found that the lesions produced in these animals were essentially the same. The observations made are well summarized in the following paragraph taken from the report of this work:⁸

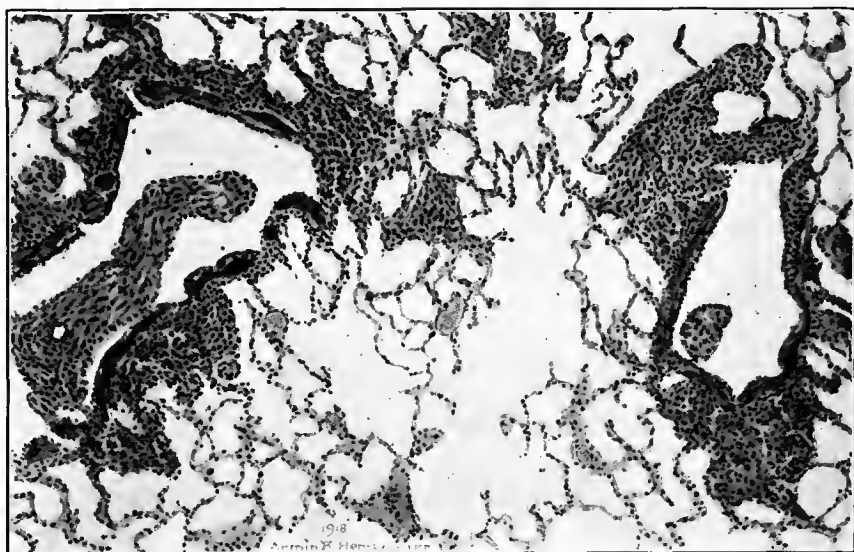


FIG. 73.—Higher magnification of two bronchi shown in Figure 72. The peribronchial thickening and the polypoid growths in the lumina are well shown

In the monkey and goat, for example, which represent the two extremes of susceptibility after exposure to the same concentration, lesions of the lung vary in degree, but not in character. The species variation, evidenced by the length of survival after gassing, depends in part upon the rate at which edema develops. On the other hand, some animals (monkey, guinea pig), the first to succumb to a given concentration, show less pulmonary edema than those that survive longer (dog, goat). This is evidence, as is brought out elsewhere just as clearly, that the edema is itself not the cause of death, but simply one manifestation of a more important underlying change.

While pulmonary edema develops more rapidly the more susceptible the species (monkey to goat) these animals—that is, the most susceptible,—show less edema than the more resistant ones.

This is an indication of the importance of the time interval in the production of the edema.

Among the investigations directed by the medical research committee of the British Army Medical Service, there is an excellent comprehensive study of the pathology of phosgene gassing in goats by Capt. J. Shaw Dunn.⁸ Certain changes found, which have not been observed in dogs, make it worth while to review here in some detail Dunn's findings.



A. ROSEN & CO

LUNGS OF DOG KILLED FOURTEEN DAYS AFTER PHOSGENE GASSING.
There is marked emphysema with irregular patches of atelectasis. Microscopically a wide-spread obliterative bronchiolitis is present.

In the first place it is pointed out that the use of goats in the study of poisoning by irritant gases affords certain advantages over most other laboratory animals.

1. The large size of the lungs permits of a much closer and more critical observation of naked-eye changes than is possible in the smaller laboratory animals.

2. The goat's lung is of a very definitely lobular construction, and in this respect is more fairly comparable with the lung of a healthy young man than those of smaller animals.

3. In goats the sequelae of gassing proceed almost invariably without septic complication, so that the phenomena observed are those attributable to the effect of the gas only.

All investigators may not agree that in the matter of size and lobulation the goat's lung has any definite advantage over the dog's lung, which is also well lobulated and quite large enough for satisfactory gross study. But certainly the relative immunity of the goat to respiratory infection made it possible to follow more easily the life history of the uncomplicated gas injury. On the other hand, it may be fairly argued that in respect to the tendency to septic complication the dog reacted much more like man than did the goat, and was therefore, for most purposes, a more suitable subject for experiment.

In general the changes found by Dunn in goats agreed with those already described in dogs, but there was one significant difference, namely, the presence of definite renal lesions.

The changes in the kidney were, in brief, a necrosis of the cells lining the convoluted tubules in the cortical labyrinth. The straight descending limbs of the convoluted tubules in the medullary rays, as well as the ascending limbs of Henle's loops, showed relatively little damage. Dunn suggests that the reason for the relative immunity of the straight tubules may depend on a different origin of their blood supply.

The renal necrosis was seen only in acute, fatal cases of gassing, and was found in only 49 out of 149 goats of this group. Similar changes were demonstrated also in acute deaths from chloropicrin.

As regards the conditions necessary to bring about renal necrosis, Dunn concluded that the lesion might be caused either by a high concentration for a short time, or by a lower concentration with prolonged exposure.¹ Artillery experiments showed that the lesion might be produced as effectively as in the gas chamber. In all cases, however, the exposure had to be lethal.

Dunn's observations on the reparative changes in the lungs agreed in most respects with those described for dogs. The rate of repair, however, was apparently more rapid in goats. Goats killed after the tenth day showed practically no trace of the gas injury beyond irregular capillary congestion and some thickening of the muscle fibers in infundibular and bronchiolar terminations, whereas in dogs, as has been pointed out, the lungs at this stage were full of fibroid nodules representing an organizing inflammatory reaction in the walls of the damaged bronchioles.

SUMMARY

Phosgene produced in animals, as in man, a widespread injury of the parenchyma of the respiratory apparatus, followed by a series of reactive phenomena which might be complicated by septic infection. The initial damage, which

¹ Renal necrosis was found also in goats killed by chloropicrin, and in two animals, exposed respectively to diphenylchlorarsine and hydrocyanic acid.

involved the lining cells of the smaller bronchi, the alveolar epithelium, and possibly also the capillary walls of the septa, was fairly uniform in distribution, differing in this respect from the commoner bacterial injuries.

The results on the organism of this injury were apparently entirely referable to local changes in the respiratory apparatus; evidences of a systemic intoxication, such as accompanies bacterial injury, were lacking.

The early inflammatory reaction consisted in a massive outpouring of fluid, in which considerable fibrin might be present. The cellular reaction, which consisted of polynuclear leucocytes and desquamated epithelium, was relatively slight. Obstruction of many of the smaller bronchial tubes was brought about by plugs of exudate and cell debris, and possibly also by irregular contractures of the muscle fibers of the bronchial wall. The result of such obstruction was partial or complete atelectasis of the area supplied by the occluded bronchus. A patchy compensatory emphysema occurred in the portions of the lung whose bronchial outlets remained patent.

In dogs and most other laboratory animals, bacterial infection frequently followed the gas injury, where death was delayed beyond 24 hours. In these cases pneumonia, generally lobular and necrotizing in character, resulted. Severe, but sublethal, exposures, not complicated by infection, led to a widespread organizing bronchiolitis, which simulated grossly miliary tuberculosis. These lesions tended to regress, ending in focal scars associated with more or less emphysema. Chronic infection of the bronchi with bronchiectasis was not an infrequent sequel of severe gassing.

No changes of any significance were found outside the respiratory tract, except in goats, where necrosis of renal tubules has been described following severe gas exposure.

PROTOCOLS

P-884.—Male brindle bull terrier; weight 13.6 kilos. August 21, 1918, gassed for 30 minutes with phosgene, 83 parts per million. Found dead 8 a. m., August 22, approximately 18 hours after gassing.

Autopsy.—Body well nourished; weight 13.2 kilos; 0.4 kilo less than weight at time of gassing. Except for a well-marked congestion of the abdominal viscera, the positive findings were limited to the respiratory tract. The lungs weigh 35 grams, with a heart-lung ratio of 2.92. The lungs are greatly distended, deep purplish red, with scattered light-colored patches along the anterior margins. The tissue is boggy and nonrepitant throughout, owing, obviously, to the extreme edema. Upon section the lung tends to collapse somewhat with the escape of much fluid.

Microscopic findings.—The alveoli throughout the lung are more or less filled with granular precipitate (edema) with considerable fibrin. Very few free cells are seen, and those present are chiefly mononuclears. The mucosa of the wall of the smaller bronchi is completely necrotic; that of the large bronchi and trachea is well preserved with cilia easily seen. The connective tissue about the larger bronchi and blood vessels is quite edematous with here and there a markedly distended lymph vessel.

Anatomical diagnosis.—Extreme edema and congestion of lungs; necrosis of bronchiolar epithelium.

NOTE.—The findings are typical of acute death from phosgene, without septic complication.

P-734.—Female black and white cur; weight 5.7 kilos. July 10, 1918, gassed 30 minutes; concentration 69 parts per million. Found dead 4.30 a. m., July 11, 1918, 18 hours after gassing.

Autopsy.—Body poorly nourished; weight 5.45 kilos. Lungs weigh 225 grams. Heart-lung ratio, 3.94, or approximately three times the normal. They are voluminous and non-

collapsible, owing to the presence of extreme edema. Congestion is less striking than the edema. The amount of residual air in the lungs is very small. The trachea and bronchi contain much frothy fluid, but the mucosa is normal looking, except for slight injection of vessels.

Microscopic findings.—Sections of the lungs show much coagulated fluid and fibrin in alveoli, distention of capillaries, edema of perivascular tissue, and dilatation of lymph channels. There is, in addition, an early bronchopneumonia, with an accumulation of polynuclear leucocytes in and about the bronchioles. Patches of greatly distended alveoli (acute emphysema) are seen near the surface of the lung. The epithelium of the smallest bronchi is quite necrotic, while that of the larger is well preserved. Sections of liver and kidney show no significant changes.

Anatomical diagnosis.—Extreme edema and congestion of lungs; necrosis of bronchiolar epithelium; early bronchopneumonia.

NOTE.—The findings are typical of acute phosgene poisoning. The case shows very clearly the earliest stage of the pneumonic reaction, which is such a conspicuous feature in most of the later deaths.

P-661.—Male fox terrier; weight 10.55 kilos. July 1, 1918, gassed 30 minutes; concentration 50 parts per million. Found dead 23 hours after gassing.

Autopsy.—Body well nourished; weight 9.53 kilos; 1.02 kilos less than at time of gassing. The lungs weigh 440 grams; heart, 100 grams; heart-lung ratio, 4.40. The pleura and trachea are normal looking. The lungs are voluminous and show the usual mottling, owing to the congestion and patchy emphysema. The tissue is very doughy and nonrepitant, with an obvious extreme degree of edema. On section small indefinitely outlined gray patches are seen about the small bronchi, suggesting an early pneumonic reaction.

Microscopic findings.—The edema, congestion, and necrosis of the bronchiolar epithelium are the conspicuous features. In and about many of the bronchioles there is a polynuclear reaction, but this is distinctly focal. Small hemorrhages involving half a dozen or more alveoli are found here and there. The epithelium of the large bronchi and trachea is well preserved; that of the smallest air passages is necrotic.

Anatomical diagnosis.—Congestion and edema of lungs, with acute compensatory emphysema; necrosis of bronchiolar epithelium; early bronchopneumonia; miliary hemorrhages in lungs.

NOTE.—The lung picture is characteristic of acute phosgene poisoning with beginning respiratory infection.

P-785.—Young female terrier; weight 5.3 kilos. July 17, 1918, gassed 30 minutes; concentration 74 parts per million. Died July 20, 1918, three days after gassing.

Autopsy.—Body is fairly well nourished; weighs 5 kilos, or a loss of 0.5 kilo. Lungs weigh 300 grams and heart 84 grams, giving a heart-lung ratio of 3.57. The lungs fill the thorax and do not collapse. The tissue is boggy and airless, except for scattered emphysematous patches. The congestion is not so striking as in the more acute deaths, but the edema is extreme, as the weight index shows. The pleura and mediastinal tissues, as well as the lung, are quite edematous. The trachea and larger bronchi are apparently unaffected and examination of the abdominal viscera is likewise negative.

Microscopic findings.—The lung shows a patchy edema with an abundance of fibrin along the alveolar walls. There is a notable absence of a cellular reaction, except for occasional desquamated epithelium in the alveoli and a few lymphocytes and plasma cells in edematous perivascular and peribronchial tissues.

Anatomical diagnosis.—Edema and congestion of lungs and mediastinal tissues; necrosis of bronchiolar epithelium.

P-676.—Brown and white male cur; weight 15.7 kilos. July 2, 1918, gassed 8.27 to 8.57 a. m., with phosgene, 51 parts per million. Found dead 8 a. m., July 6. Degree of post-mortem change indicated that death had occurred about six hours previous, or approximately three and a half days after gassing.

Autopsy.—Body is poorly nourished but not emaciated; weight 14.16 kilos, or 1.54 kilos less than before gassing. Heart weighs 175 grams. It is filled with mixed red and white clot. There are no endocardial hemorrhages. Except for moderate distention of the cham-

bers, nothing noteworthy is found. The left pleural cavity contains a small quantity of blood-stained pus; while in the right cavity several hundred cubic centimeters of clear fluid is present, compressing the right lung. Lungs: Right weighs 140 grams; left 430 grams. The left lung is quite voluminous, deeply congested, but strikingly mottled owing to the presence of pale emphysematous patches throughout the organ. The upper lobes are moderately crepitant with scattered firm areas; the lower are firm and nodular throughout. On section, numerous patches of typical bronchopneumonia, tending to become confluent, are seen in the lower lobe, and similar, smaller and more scattered foci in the upper lobe. The right lung is small, firm and tough, and airless; the typical picture of pressure atelectasis. The trachea and larger bronchi show no gross change, except a slight congestion and some excess of mucus. The liver, kidneys, and spleen, which weigh, respectively, 725 grams, 58.6 grams, and 42 grams, are not grossly altered. Cultures of left lower lobe of lung show a *Staphylococcus aureus*.

Microscopic findings.—The only significant findings are in the lungs. The picture varies in different portions. In the left upper lobe there is an early bronchiolitis with an interstitial reaction increasing the thickness of the septa. In the lower lobe, widespread pneumonic reaction is present. Atelectasis is the most marked change in the right lung. There is slight edema throughout. The mucosa of the medium-sized and large bronchi is well preserved; in the smaller air passages the layer of ciliated epithelium is lost. The deeper layer of cells shows evidence of active regeneration.

Anatomical diagnosis.—Bronchopneumonia (left) with beginning organization; empyema (left); hydrothorax (right) with atelectasis of right lung; moderate edema and congestion; patchy compensatory emphysema.

NOTE.—This is a typical instance of delayed death from respiratory infection.

P-738.—Young male terrier; weight 5.9 kilos. July 10, 1918, gassed 30 minutes with phosgene; concentration 61 parts per million. Died, July 15, 1918, five days after gassing.

Autopsy.—Body is poorly nourished; weight 4.9 kilos; that is 1 kilo less than at time of gassing. The heart weighs 125 grams full of blood; 75 grams empty. It contains chicken-fat clot. Endocardium and myocardium normal looking. Lungs weigh 250 grams, giving a heart-lung ratio of 3.33. The lungs are very voluminous with a smooth, shiny pleura. They are moderately congested, very heavy, but not strikingly edematous. The tissue is firm and nodular throughout, with crepitation in patches only. On section the nodules are seen as poorly defined patches scattered through all lobes. There is no pus or other exudate in the larger bronchi or trachea. Lung cultures showed a *Streptococcus hemolyticus*.

Microscopic findings.—Throughout the lung there is considerable edematous fluid in the alveoli and the capillaries are everywhere congested. Fibrin is abundant. Special fibrin stains show dense blue masses of old fibrin adherent to the alveolar wall. In and about the smaller bronchi, there are many polynuclear leucocytes. Elsewhere there are only a few cells in the alveolar spaces, and these are chiefly mononuclears. The lining epithelium of the smaller bronchi is entirely lost and the lumina are filled with cellular debris. Sections of liver, spleen, and kidney show moderate congestion but no other change.

Anatomical diagnosis.—Edema and congestion of lung; focal and diffuse interstitial bronchopneumonia.

NOTE.—The reaction of the lung in this case was strikingly proliferative, and suggests a response to a chemical rather than a bacterial injury. The presence of streptococci, however, indicates a double injury.

P-641.—Male brown bull; weight 12.4 kilos. June 28, 1918, gassed for 30 minutes with phosgene; 53 parts per million. Died, July 6, 1918, eight days after gassing.

Autopsy.—Body well nourished; weight 11.6 kilos, 0.8 kilo less than weight at time of gassing. The heart weighs 185 grams full of blood, 120 grams empty. There are no hemorrhages in the endocardium and no myocardial changes. The lungs weigh 475 grams with a heart-lung ratio of 3.95. The lungs are quite voluminous and on palpation are nodular in all lobes. The tissue is moderately congested and slightly edematous. There are a few patches of acute emphysema. There are no hemorrhages. The nodules felt are seen on section as dry gray patches, fairly sharply defined. There is no exudate in the bronchi, apart from the expressed edema fluid.

Microscopic findings.—There is a widespread edema and congestion of the lungs. The fibrin is abundant and forms a dense layer on many of the alveolar walls. The septa are diffusely thickened owing to active proliferation of fibroblasts. In places there is a polynuclear cellular reaction in the smaller bronchi and adjacent alveoli, but much more conspicuous is the proliferative interstitial reaction. The epithelium of the smaller air passages is lost with here and there evidence of regeneration. In general the lining cells of the larger bronchi are intact, but in a few places a focal damage is seen.

Anatomical diagnosis.—Edema and congestion of lungs; necrosis and regeneration of bronchiolar epithelium; organizing interstitial pneumonia.

P-813.—Male collie. July 25, 1918, gassed 30 minutes; concentration, 87 parts per million. Recovered. Killed with strychnine August 6, 1918, 12 days after gassing. Condition when killed, good; looks well and is fairly lively.

Autopsy.—Body well nourished; weight, 13.6 kilos. No changes of any consequence are found except in the lungs, which show an organizing bronchiolitis of the type seen in P-668, though somewhat less marked; that is, the nodules are not so numerous. A few fresh hemorrhages are found in the pleura and lung. These obviously occurred in the death struggle.

Anatomical diagnosis.—Organizing bronchiolitis; recent pulmonary hemorrhages.

NOTE.—The findings are fairly typical of those in animals which were recovering from severe gassing. The lesions were obviously undergoing regression and are much less conspicuous than in dogs killed after several months, except in cases where a complicating pulmonary infection had occurred.

P-767.—Young female hound; weight, 6 kilos. July 15, 1918, gassed 30 minutes; concentration, 65 parts per million. Died, August 1, 1918, 17 days after gassing.

Autopsy.—Body poorly nourished; weight, 4.6 kilos. Except for a moderate degree of anemia of all tissues, significant changes are found only in the lungs. They weigh 175 grams, with a weight index of 3.43. There are widespread consolidated patches in all lobes, but most marked in the upper. On section the picture is a typical confluent bronchopneumonia with considerable edema and congestion.

Microscopic findings.—The bronchi form the centers of many of the pneumonic patches. There is a proliferation of fibroblasts in the alveolar walls in places, but in general the inflammatory process looks quite recent.

Anatomical diagnosis.—Organizing bronchopneumonia; edema and congestion of lungs.

NOTE.—The case is an example of the development of a fatal pneumonia some time after the subsidence of the acute reaction following gassing.

P-668.—Female yellow hound. July 1, 1918, gassed 30 minutes; concentration, 55 parts per million. Recovered; regassed July 27; concentration, 74 parts per million. Killed with strychnine August 16, 1918, 36 days after first gassing, and 10 days after second gassing. Condition when killed, well nourished, lively, and apparently healthy, except for mange.

Autopsy.—Body weight, 14.5 kilos. Heart weighs 175 grams full, and 100 grams empty. The only significant positive findings are in the lungs. They weigh 275 grams, giving a heart-lung ratio of 2.75, and are moderately but irregularly collapsed. The anterior margins of the upper lobes are atelectatic. The pleura is thin and smooth, but here and there fresh subpleural hemorrhages are seen. While the lung tissue is crepitant throughout, numerous small firm nodules are felt. On section these are seen as indefinitely outlined red or gray foci. In many of the nodules recent hemorrhage is seen. There is no edema or congestion and no exudate in the bronchi.

Microscopic findings.—The number and uniform size of the nodules in the lungs, as they appear in the sections without magnification, suggest a miliary tuberculosis. Under the microscope, however, the lesion is seen to be an organizing bronchiolitis of the type shown in Figures 72 and 73. There is no leucocytic reaction and no fibrin or edema. The picture suggests a healing gas injury rather than a persistent bacterial infection.

Anatomical diagnosis.—Widespread organizing bronchiolitis ("pseudo-tuberculosis").

NOTE.—The extent of the pulmonary lesions in this case was greater than in the majority of recovered dogs and was probably due to the double exposure.

DIPHOSGENE (TRICHLOROMETHYLCHLOROFORMATE)

Diphosgene (ClCOOCCl_3), better known as "superpalite," is closely related chemically to phosgene (COCl_2). It is therefore not surprising to find that the lesions produced in animals by the two gases are practically identical. Another closely related compound, chloromethylchloroformate, better known as "palite," also produces effects which are not distinguishable from those of phosgene. Since the pathology of phosgene has been fully discussed, we shall give here only a brief summary of the studies made by Winternitz and Wislocki,¹⁰ in the American University laboratories, leaving the interested reader to consult the original report for details.

Studies were made of changes in 35 gassed dogs, of which 21 succumbed within 3 days after gassing, and 9 from 3 to 14 days. Five dogs recovered and were killed 2 weeks to 3 months after gassing.

As with phosgene gassing, there was a latent period after exposure in which no deaths occurred. The earliest death was 8 hours after gassing, while the majority of animals succumbed between 12 and 36 hours.

In the acute deaths, pulmonary edema and congestion, and patchy emphysema were the most striking gross features. Histological studies showed that, as in phosgene, the trachea and larger bronchi were spared, the chief seat of injury being the distal portion of the respiratory apparatus—that is, bronchioles and alveoli.

Dogs that survived the acute stage were very prone to respiratory infection, and deaths occurring after two days were practically all due to pneumonia.

A study of the lungs of recovered dogs showed the same residual lesions—bronchiolar scarring, patchy emphysema, chronic bronchitis—that were observed in phosgene dogs.

CHLOROPICRIN (CCl_3NO_2)

While chloropicrin belongs to the respiratory irritant group of gases, it has certain properties which set it apart from the other members of this group. In the first place, it is not a gas but a liquid with a fairly high boiling point (112°C). Furthermore, in contrast to phosgene and chlorine, it is very stable and nonabsorbable, and while in its deleterious action on tissues decomposition undoubtedly takes place, the nature of the change is not known.

Direct application of the liquid to the skin produces severe, deep burns, and a drop on the cornea results in ulceration. Inhalation of the gas leads to respiratory and circulatory disturbances, closely resembling those associated with chlorine and phosgene gassing, already described. Tendency to nausea and vomiting, apparently from the irritation of the stomach by the swallowed gas is more common than with the other war gases, though not constant, except where high concentrations are used.

A systematic study of the pathology of chloropicrin gassing was made in the Yale laboratories¹¹ through cooperation with other workers, who were investigating other phases of the gas action. The following report is based on the observations thus obtained.

MATERIAL

There were, altogether, 120 gassed dogs, upon which autopsies were performed. Histological as well as gross studies were made in all cases.

TABLE 55.—*Dogs gassed with chloropicrin*

Time of death after gassing	Died	Killed	Total
First 12 hours	38	1	39
12 to 24 hours	19	4	23
Second day	15	2	17
Third day	9	0	9
Fourth day	1	8	9
Fifth to tenth day	2	2	4
Eleventh to twenty-sixth day	8	8	16
	92	25	117

Table 55 shows the number of deaths in successive days after gassing, and in Chart XXVII there is a curve based on these figures. It is seen that, as with corresponding lethal exposures to chlorine and phosgene, the first 24 hours after exposure was the critical period, the largest number of deaths

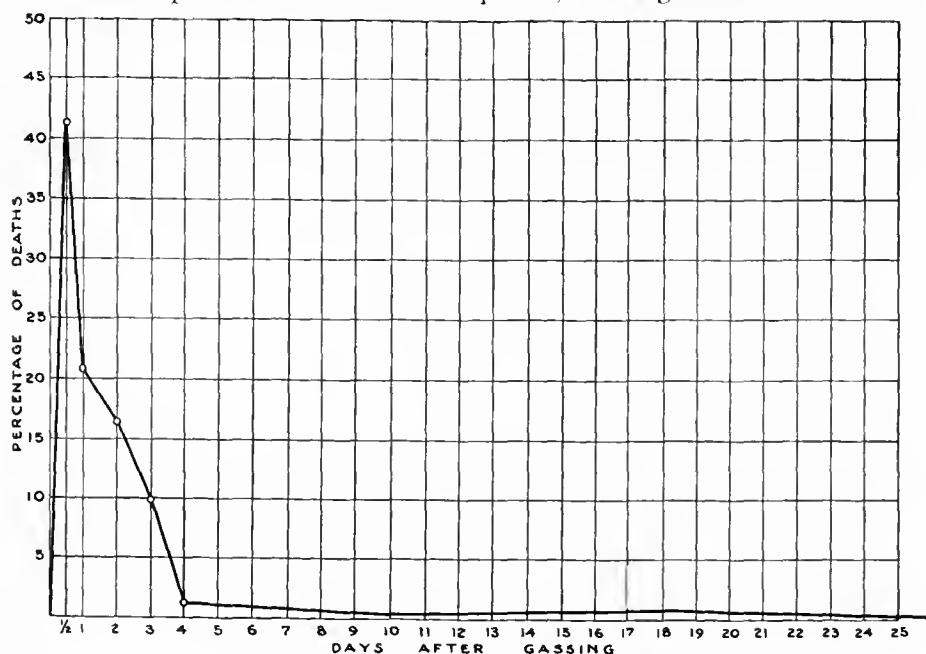


CHART XXVII.—Duration of life after chloropicrin gassing

occurring during this time. The first part of the curve is not like the curves for chlorine and phosgene, in that in the former the peak is reached in the first 12 hours, instead of the second 12 hours, as is the case with the latter. However, there is not the secondary rise on the third and fourth days, noted in the chlorine series.

No figures, as to the number of animals which survived gassing, are given, but it may be stated that in general a fairly large percentage of animals survived exposure to concentrations of 60 to 80 parts per million, whereas a half hour's exposure to somewhat higher concentrations (125 to 150 parts per million) gave a mortality of more than 50 per cent.

AUTOPSY FINDINGS

The changes found at autopsy, as might be expected, were quite similar in many respects to those produced by chlorine, phosgene, and other members of the respiratory irritant group.

Since the experimental pathology of chlorine and phosgene has been discussed in some detail in the following description, frequent comparisons will be drawn of the differences between the lesions produced by those gases and chloropierin.

We may conveniently divide the discussion into the findings in animals dying (1) in the acute stage and (2) in the subacute and chronic periods.

DEATH IN ACUTE STAGE

We have applied the expression "acute stage" somewhat arbitrarily to the first 24 to 48 hours after gassing, during which time the signs and symptoms were chiefly those of edema of the lungs, without definite evidence of infection.

PROTOCOL

The following protocol will illustrate very well the usual findings at this period:

Young Airedale, female; weight 11.1 kilos; gassed September 26, 1918, 30 minutes; concentration 1.035 mgn. per liter.

Typical symptoms during and after gassing: Lacrymation, retching and vomiting; depression. Later, viscid frothy discharge from mouth and nose, rapid and labored breathing, restlessness. Death, 15 hours after gassing.

Autopsy.—Three hours after death. Body is well nourished, but flanks and abdomen are shrunken. Weight is 700 grams less than at time of gassing. Body is lax; there are beginning post-mortem changes.

Abdomen.—Negative, except for engorgement of veins and congestion of liver. The congestion disappears as vessels are cut, the organ assuming normal color, with usual distinct lobulation.

Thorax.—The cardiac area is large; the pericardial sac is tense, being stretched by the distended heart. Lungs are bulky, but do not tend to overlap the heart. There is a slight excess of fluid in pleural cavities and pericardium. Tissues about the great vessels are slightly blood stained.

Heart.—Weighs, full of blood, 130 grams; empty, 83 grams. Heart-body ratio is approximately 0.008, that is, about normal. The right side is more distended than the left. Chambers are filled with red clot. The heart valves are normal. Beneath the endocardium of the left ventricle there are three or four hemorrhagic patches 1 to 3 mm. wide, and extending 0.5 to 1 cm. along the crests of the muscular ridges. The heart is otherwise normal.

Lungs.—Weight, 320 grams; volume, 330 c. c. The lungs are voluminous but not extremely so. Pleura is smooth, but looks thick and slightly opaque (edematous), giving the suggestion of a film over the lung. The lungs are unusually colored, being a dusky, bluish red or pink, distinctly cyanotic, with a semitranslucent quality over all. Here and there are light whitish patches, but these are neither large nor numerous (as in phosgene poisoning). In such patches there is crepitation, but practically everywhere else the lung is doughy and airless. On section, clear fluid and blood pour out like water from a squeezed sponge. The tissue is red and semitranslucent, with occasional lighter, air-containing patches. Near the margins of the upper lobes there are a few small emphysematous areas. The bronchi, like the lung proper, are full of fluid, and in the large branches there is some froth. The mucosa is somewhat reddened, and that of the smallest branches is rather opaque. About each there is a zone of edema, which is also conspicuous about the larger blood vessels. The trachea is full of sticky froth. Its mucosa is slightly reddened but is otherwise normal.

Examination of the remaining organs, liver, spleen, kidneys, adrenals, gastrointestinal tract, brain, is negative.

Microscopic findings.—There are no noteworthy changes except in the respiratory tract. The tracheal epithelium is practically everywhere intact, but in places the superficial cells are somewhat shrunken and distorted and have lost their cilia; a few are desquamated. In the largest bronchi a similar condition is seen; but as one passes downward into the medium-sized cartilage-containing tubes, the injury is far more serious. The superficial cells are quite necrotic, and the entire layer is partially loosened from the wall. (Fig. 74.) In the bronchioles and atria there is not only death of the lining cells but necrosis of the wall itself.

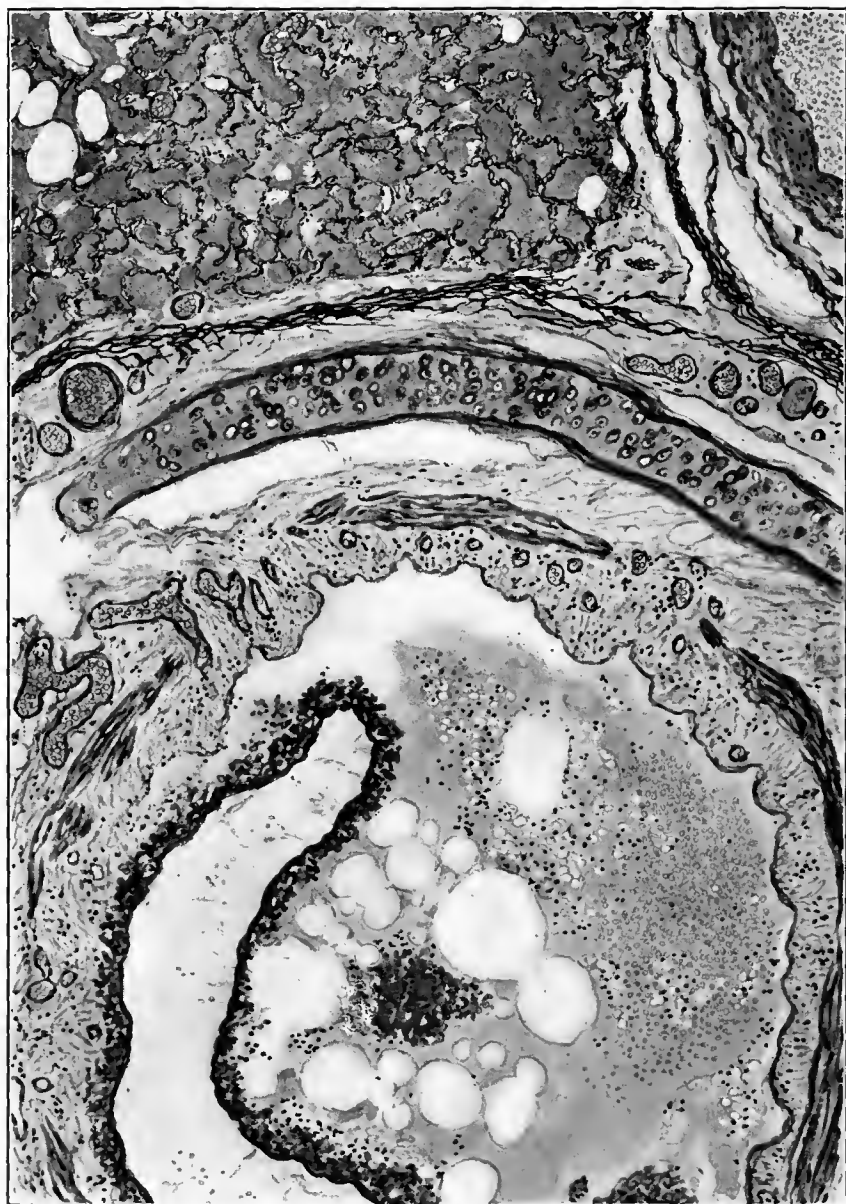


FIG. 74.—Necrosis of bronchial epithelium and subepithelial edema in acute death from chloropicrin gassing

The lung tissue shows practically everywhere a complete filling of the alveoli with coagulated edematous fluid, which is quite rich in albumin. (Fig. 75.) A few air bubbles are seen, but these are more prominent in the bronchial fluid. Desquamated alveolar cells are fairly numerous. There is some fibrin free in the alveoli, and covering the septa everywhere, like vines on a lattice, are dense strands.

Special stains show that the fibrin threads permeate the alveolar walls interrupting the capillary bed, as has been demonstrated in phosgene and chlorine poisoning. This permeation is most marked in and about the walls of the bronchioles where the damage to the tissue is greatest.

Anatomical diagnosis.—Extreme edema and congestion of lungs; necrosis of bronchial epithelium and bronchiolar walls; dilatation of heart; passive congestion of abdominal viscera.

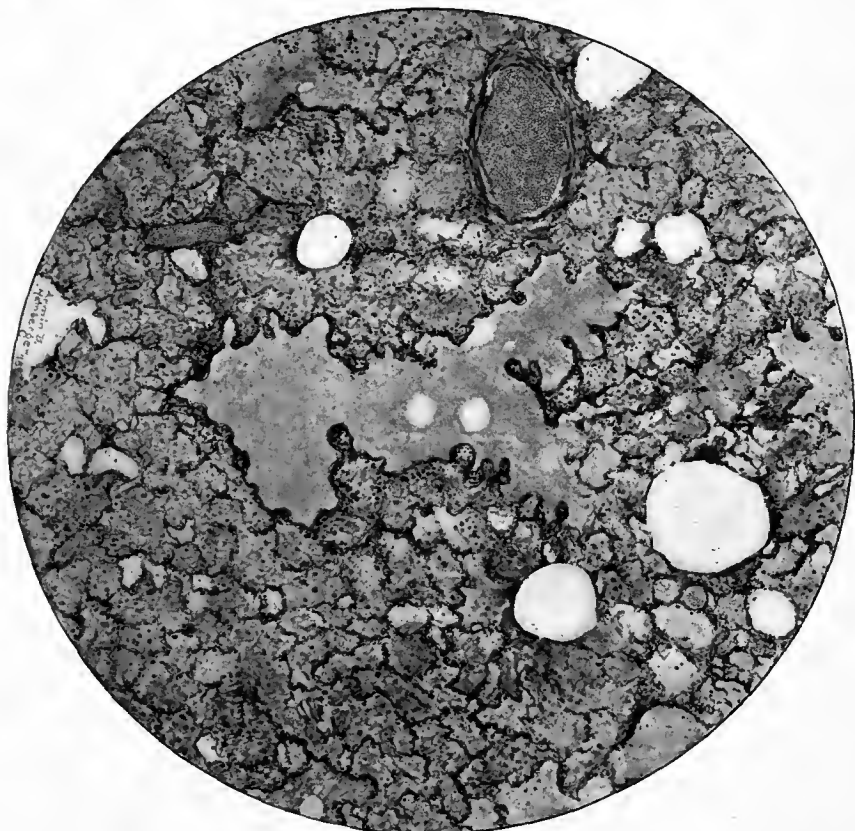


FIG. 75.—Widespread edema of lung associated with acute death from chloropicrin. Note occasional clear spaces (air bubbles) in some of the alveoli

The findings in the case just described are quite typical of acute chloropicrin death. There was little difference in the picture whether the animal died 4 hours or 24 hours after gassing, except that in those living longer an early inflammatory reaction was generally found. More will be said of this in connection with the "delayed deaths."

There was in all of these early deaths an overwhelming edema of the lungs, which constituted the most striking feature of the autopsy findings. The degree of edema, as judged by the lung-heart and lung-body weight ratios, varied considerably with individual animals, but the average for dogs dying in the first, second, or third 6-hour period was practically the same. This

might suggest that death ensued in each particular case when a certain degree of edema was reached. But an analysis of the figures obtained from dogs which were apparently recovering, killed 18 to 48 hours after gassing, shows that among these the degree of edema, based on the proportionate weight of the lungs, heart, and body, was as great as in the animals that died. In other words, the presence of any definite quantity of fluid in the lung did not seem to be the cause of death. This idea has been substantiated experimentally by Winternitz and Smith,¹² in their studies upon pulmonary irrigation. This question will be considered in a later part of this chapter dealing with the more important phenomena of the gassed state.

DEATH IN THE SUBACUTE OR CHRONIC PERIOD

The proportion of animals dying on any one day after the first 48 hours was relatively small (See Table 55), but the total number of these "delayed deaths" was considerable in any large series of experiments. The cause of death was in almost every instance a superimposed respiratory infection. This might begin within a few hours after gassing, but generally did not become widespread for several days. In some instances the infection ran a chronic course, killing only after weeks or even months, in which cases a suppurative bronchitis with more or less organizing pneumonia was generally found.

Dogs dying 2 to 10 days after gassing usually showed a purulent bronchitis and bronchopneumonia. (Fig. 76.) Several lobes were almost always affected. Occasionally, patches of consolidation were found throughout the entire lung. The upper lobes were more often involved than the lower. This may be accounted for either by the greater dependency of the upper lobes in four-footed animals, or by the poorer drainage due to the more abrupt branching of the bronchi. There was a somewhat greater tendency to abscess formation and extension of the infection to the pleura than after phosgene gassing. Organization of the pneumonic exudate occurred frequently.

TABLE 56.—*Dogs gassed with chloropicrin—per cent showing pneumonia*

Dogs dying:	Per cent
First 12 hours.....	27
12 to 24 hours.....	45
Second day.....	60
Third day.....	63
Fourth day.....	100
Fifth to tenth day.....	100
Eleventh to twenty-sixth day.....	71

It will not be necessary to describe the gross and microscopic findings in these cases since they were practically the same as in chlorine and phosgene poisoning, which have been fully discussed in the preceding pages.

RECOVERED ANIMALS

Twenty-five animals, which had survived exposure to a lethal^a concentration of chloropicrin, were killed at different periods after gassing. (See Table 55 for detailed figures.) These exhibited very clearly the nature of the reparative processes which follow the gas injury.

^a The term "lethal" is applied here to concentrations which, in a given period kill the majority of exposed dogs.

The edema began to regress after about two days, but at least a week was required for its complete disappearance. It may be mentioned in this connection that the quantity of fluid present in the lungs in some of the two and three day dogs, in which all untoward symptoms had disappeared, was found to be as great as in the dogs which had died. There was, however, a greater quantity of residual air in the lungs, as shown by a comparison of the weights and volumes.

Fibrin in the alveolar spaces and walls was removed rather slowly, old strings and plugs of it being demonstrated sometimes seven or eight days after gassing.

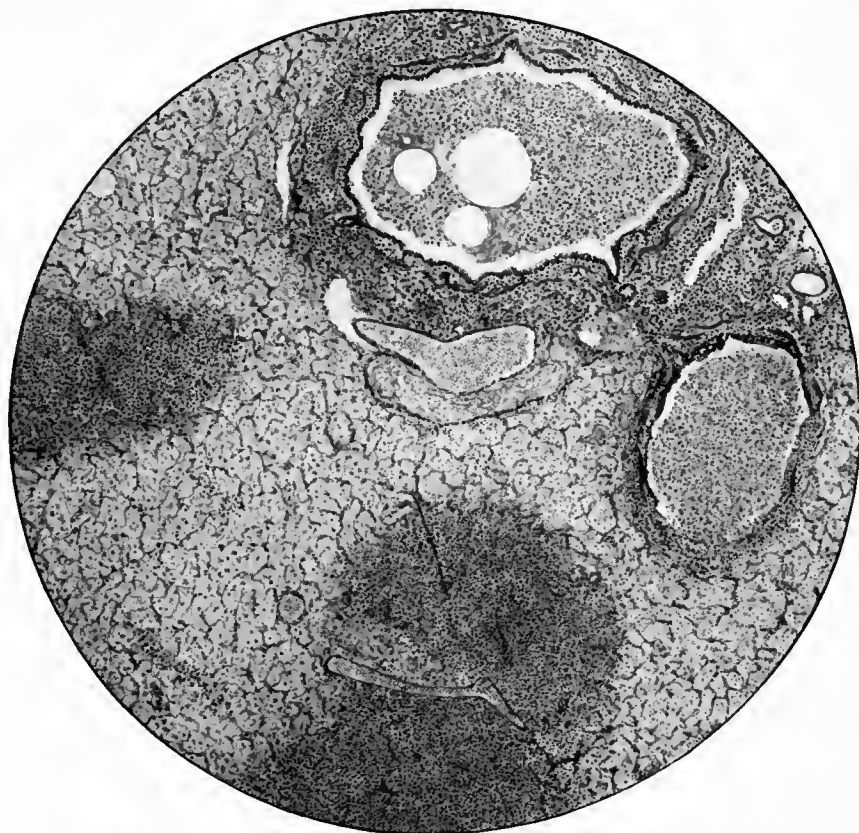


Fig. 76.—Acute bronchitis and bronchopneumonia causing death three days after exposure to chloropicrin. The lung tissue separating the pneumonic patches is markedly edematous

Where the bronchiolar walls had been seriously damaged, and this happened quite regularly after exposure to high concentrations, and active proliferation of fibroblasts began about the dead area as early as three days after gassing, and the bronchial cavity was soon filled with granulation tissue. The final picture was that of an obliterative bronchiolitis, as described in chlorine and phosgene gassing.

Regeneration of the bronchial and alveolar epithelium proceeded quite rapidly. It was best seen in dogs which had been exposed to sublethal concentrations of the gas, where only the superficial layer of cells had been killed.

In sublethal exposures, there were present quite regularly curious structures in the alveolar spaces, which under low magnification looked like giant cells. Under greater magnification they had the form of capillaries, although one found in all only disintegrated red blood cells and fibrin, and no fresh blood. One was inclined, at first, to interpret these structures as foreign-body cells, which were formed about masses of cell débris and fibrin, but a more careful study showed that they were attached to the alveolar wall and were probably sections of bulging capillary tufts which had become thrombosed.

TABLE 57.—*Dogs gassed with chloropicrin—degree of edema of lungs*

No.	Breed	Sex	Concentration	Death, hours after gassing	Body weight (grams)	Heart weight	Lung			
							Volume	Weight	Difference	Weight index
1	Cur.	Male	1.039	4	10,400	76	415	400	15	4.04
2	Collie	do.	.985	6	11,800	120	635	465	70	2.98
3	Bull.	do.	1.070	13	10,400	80	450	375	75	3.60
4	Cur.	do.	.992	12	13,600	125	400	335	65	2.06
5	do.	do.	.930	5	19,500	175	510	510	0	2.26
6	Collie	do.	.891	8	13,400	95	375	355	20	2.87
7	Mongrel.	Female	.906	8	9,300	90	300	245	55	2.09
8	Cur.	Male	.819	7	900	105	360	320	40	2.34
9	Collie	do.	.985	12-24	11,350	105	425	350	75	2.56
10	do.	do.	1.107	12-24	15,900	100	400	350	50	2.69
11	Cur.	do.	1.029	12-24	9,800	105	350	300	50	2.19
12	Collie	do.	1.075	12-24	15,400	140	500	450	50	2.47
13	Cur.	Female	1.015	12-24	10,400	80	310	300	10	2.88
14	do.	Male	.991	9	10,400		390	350	40	
15	Coach dog.	Female	1.034	4	9,000	65	420	345	75	4.07
16	Cur.	Male	1.064	8	8,340	95	300	225	75	1.81
17	do.	Female	1.017	9	7,000	62	290	225	65	2.79
18	do.	Male	1.006	7	8,100	75	325	290	35	2.97
19	Airedale	Female	.911	12-24	13,160	150	575	525	50	2.70
20	Cur.	Male	.983	5	7,000	60	300	225	75	2.88
21	Mongrel.	do.	.890	12-24	7,900	75	350	250	100	2.56
22	Cur.	Female	.999	12-18	8,500	75	300	275	25	2.81
23	do.	Male	1.020	8	8,800	75	300	275	25	3.79
24	do.	do.	1.041	12-18	9,300	96	400	350	50	2.79
25	Airedale	do.	1.015	10	9,300	127	280	250	30	1.51
26	Poodle	do.	1.087	7	8,200	84	225	205	20	1.87
27	Cur.	do.	1.046	8	12,900	130	375	365	10	2.16
28	Collie	do.	.891	26	16,000	125	480	300	180	1.85
29	do.	do.	.752	20	18,000	151	480	410	70	2.04
30	Cur.	do.	.908	8	10,000	102	310	280	30	2.12

NOTE.—Data indicating the degree of edema of lungs and acute emphysema in dogs dying acutely after chloropicrin gassing. The extent of the edema may be judged by the weight index in the last column. Index is obtained by dividing the lung weight by the heart weight, and this quotient by 1.30, the normal proportion. The weight index thus represents the degree of increase in lung weight. The great variation in the figures, 1.51 to 4.07, is significant (see text). The slight differences in the weight and volume of the lungs show the small amount of residual air present as compared with phosgene and superpalite gassing.

SUMMARY

Chloropicrin, like chlorine and some of the other gases of the respiratory irritant group, injured the epithelium of the entire respiratory tract, but all portions of the tract were not equally affected. The trachea and largest bronchi, though irritated, suffered only slight and transient injury. The medium-sized and small bronchi were most affected. There was a uniform, widespread damage of the alveolar walls, which, however, was not severe enough to lead to necrosis. The alveoli were apparently nowhere protected by constriction of the bronchi.

An overwhelming edema of the lungs rapidly followed exposure to lethal concentrations of the gas. In extreme cases practically every alveolus was filled with fluid, so that at autopsy the weight and volume of the lungs (expressed in grams and cubic centimeters) approximated one another. In addition to the fluid in the lung itself, there was also marked edema of the mediastinal tissues and pleura, which was even more striking than in phosgene and chlorine

gassing. The edema fluid contained fibrin in places, and a great deal of fibrin was found in the alveolar walls. It was especially abundant in dogs that had lived at least 24 hours.

Partial or complete occlusion of the smaller bronchi by inflammatory exudate or masses of necrotic desquamated cells led to focal emphysema or atelectasis, but this was not such a striking feature at autopsy as in death from some of the other respiratory irritant gases (phosgene, superpalite).

Infection of the lungs, with the development of a widespread bronchitis and bronchopneumonia, was seen in a large percentage of the severely gassed animals which did not die in the first few hours after gassing. Abscess formation, pleurisy—fibrinous or purulent—and organizing pneumonia were common complications. In recovered animals there was a regeneration of the epithelium of the bronchi and alveoli, and organization of the necrotic bronchiolar wall, with scar formation (obliterative bronchiolitis). Focal atelectatic and emphysematous patches remained as permanent gross evidence of the gas injury.

A study of "recovering" animals killed at different periods indicated that the cause of death in the early stage—that is, before infection had become well established—was not due to the edema per se but probably to obstruction of the blood flow through the lungs caused by extensive deposition of fibrin in the alveolar walls. The increased viscosity of the blood from the loss of fluid into the lungs, emphasized by Underhill,⁵ was no doubt also a very important factor. Likewise some of the "delayed deaths" were to be attributed to this obstruction in the pulmonary circulation, but the great majority were obviously due to an infection of the lungs, bronchi or pleura.

PROTOCOLS

C. P. 34.—Brown and white male mongrel; weight 13.1 kilos. Gassed, August, 23, 1918; 30 minutes exposure to chloropicrin; 169.3 parts per million. Greatly excited during exposure, jumping around and licking nose. Toward the end there was vomiting and urination. Half hour later, pulse 60, respirations 16, temperature 39.2°. Eight hours later pulse 132, respirations 68, and temperature 38.6°; hemoglobin 229 per cent. Death occurred 10 hours after exposure.

Autopsy.—Body weight 12.5 kilos (a loss of 0.6 kilo). The lungs weigh 375 grams, the heart 125 grams, giving a heart-lung ratio of 3. The lungs are mottled and voluminous, and quite doughy. They are airless in the entire lower lobes and the greater part of the upper lobes. Crepitation is felt only along the margins of the upper lobes. There are a few sub-pleural hemorrhages.

Microscopic findings.—The lungs show a widespread edema, the fluid in the alveoli being particularly rich in albumin, as indicated by the deeply staining coagulum. (See Fig. 75.) There is practically no cellular reaction. The mucosa of the bronchi is quite necrotic and sloughing; that of the trachea is damaged with partial desquamation in places, but no reaction except marked vascular congestion.

Anatomical diagnoses.—Congestion and edema of lungs; necrosis of bronchial epithelium.

NOTE.—The case illustrates well the intermediary position of the lesions of chloropicrin when compared with those of phosgene and chlorine. The trachea, for example, was damaged much more than in gassing by phosgene, but much less than was seen after fatal exposures to chlorine.

C. P. 35.—Female coach dog; weight 15.4 kilos. Gassed, August 23, 1918; 30 minutes exposure to chloropicrin; 164.9 parts per million. Dog took gas well, showing very little disturbance. Before exposure, pulse 66, respirations 36, and temperature 38.3°. Six hours after gassing, pulse 124, respirations 24, and temperature 38; hemoglobin 213 per cent. The dog was found dead 12 hours after gassing.

Autopsy.—Body weight was 14.1, a loss of 1.3 kilos. The lungs weigh 490 grams; heart weighs 175 grams; heart-lung ratio 2.8. The lungs are dark purple, with a slight mottling in the upper lobes. There is edema throughout, with extreme congestion. Only a few patches of emphysema are present and these are limited to the upper lobes. There are no hemorrhages or pneumonic foci. The trachea and bronchi show congested mucosæ, but no membrane formation.

Microscopic findings.—There is extreme congestion and edema in the lungs, with no pneumonia. Changes are practically the same as in C. P. 34, described above.

C. P. 93.—Boston bull; weight 7.15 kilos. September 9, 1921, gassed 30 minutes with chloropicrin; 0.697 mgm. per liter. During exposure vomits, licks nose and chops, and keeps eyes closed. Found dead on morning of September 11, two days after gassing.

Autopsy.—Body weighs 5.5 kilos (loss of 1.65 kilos after gassing). Heart weighs 55 grams, lungs 310 grams; heart-lung ratio 5.63. Lungs are heavy and voluminous, with well-marked edema and congestion, in addition to firm, confluent pneumonic areas which are felt in all lobes. Trachea looks unchanged except for slight congestion.

Microscopic findings.—A typical bronchopneumonia is found such as is shown in Figure 76. The bronchi are filled with purulent exudate and necrotic epithelium.

Anatomical diagnoses.—Edema and congestion of lungs; necrosis of bronchial epithelium; bronchopneumonia.

NOTE.—The findings are typical of those generally seen in delayed deaths. The respiratory infection dominates the picture.

C. P. 6.—Black and brown male hound; weight 14 kilos. Gassed, August 16, 1918; 30 minutes exposure to chloropicrin, 103.5 parts per million. There was retching and vomiting during exposure, with salivation and discharge from the nose. One hour later, pulse 68, respirations 38, and temperature 38.5°. Condition did not appear serious, and three days later dog was sent to the Brady Laboratory showing no symptoms. Dog was killed with chloroform.

Autopsy.—Body weighs 12.5 kilos, which is 1.5 kilos less than at time of gassing. Lesions are found only in the lungs. They weigh together 190 grams, with a heart-lung ratio of 1.79. The lungs are somewhat mottled and voluminous. All lobes are more or less doughy and on section exude fluid. A few scattered hemorrhages are seen.

Microscopic findings.—Only subacute changes are found. There is active regeneration of the lining epithelium of the smaller bronchi and bronchioles. The bronchial walls are quite cellular, from the presence of both fibroblasts and mononuclear wandering cells. Nearly every bronchus shows hemorrhagic extravasations, as is very well shown in Plates XIII and XIV. In the alveoli about the small bronchi are many large phagocytic cells, and occasional capillary-like structures such as is seen in Figures 77 and 78. On the whole, the fibroblastic reaction is not as marked as is generally seen after chlorine and phosgene gassing.

Anatomical diagnoses.—Organizing bronchiolitis with hemorrhages; degeneration of bronchial epithelium.

NOTE.—The hemorrhages in this case were evidently terminal occurring during the death struggle. The other lesions were probably regressive and would have gone on to healing.

COMPARISON OF THE ANATOMICAL CHANGES PRODUCED BY CHLORINE, PHOSGENE, AND CHLOROPICRIN

Chlorine injures by combining directly with the cytoplasm of exposed cells, or through the formation of hydrochloric acid, which, in turn, acts on the tissues. Phosgene, COCl_2 , coming in contact with water, rapidly decomposes, with the liberation of hydrochloric acid, HCl , which constitutes the toxic agent. Chloropicrin is very stable in vitro, and it has not yet been determined just how it reacts with tissues to injure them; but it seems likely that, as in the case of phosgene, its toxicity is referable to the chlorine part of its molecule, which is in some way split off as the gas reaches the tissue.

It would appear, therefore, that with each of the three gases the directly injurious agent is the same—chlorine—and that their pathologic effects should be very similar. The description of the lesions produced in dogs by the three gases, as given in the preceding pages, shows that this assumption is correct. There were, however, certain points of difference, which are sufficiently clear-cut to enable an experienced observer to say from an examination of the organs of a gassed animal which of the three gases had been used.

LOCUS OF INJURY

Chlorine damaged, and in high concentration entirely destroyed, the epithelial lining of the upper portion of the respiratory tract—trachea, large

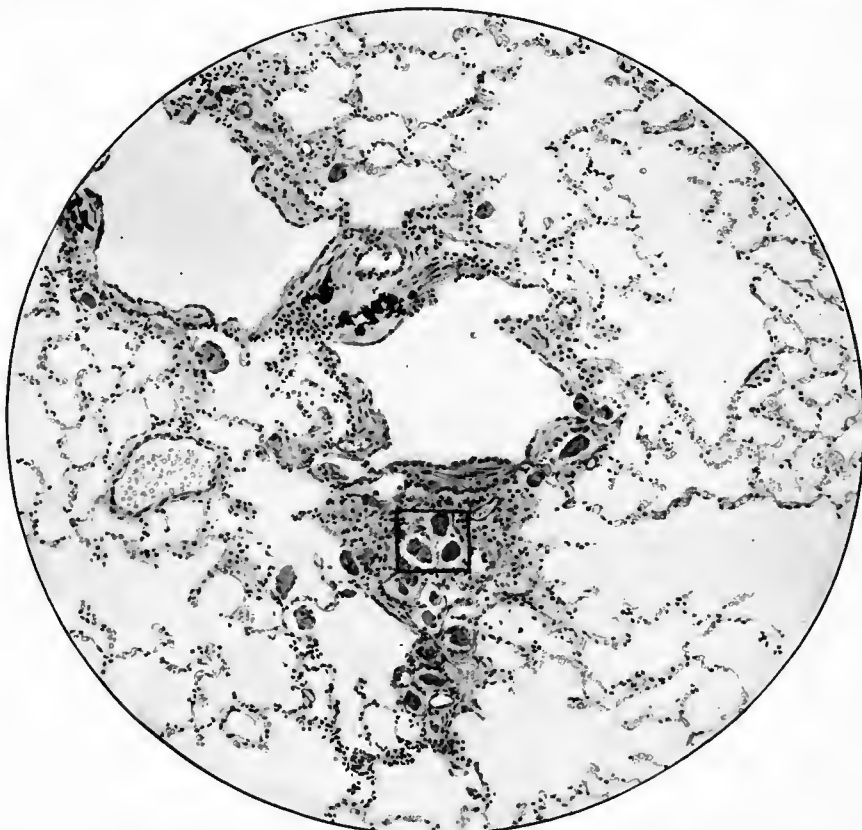
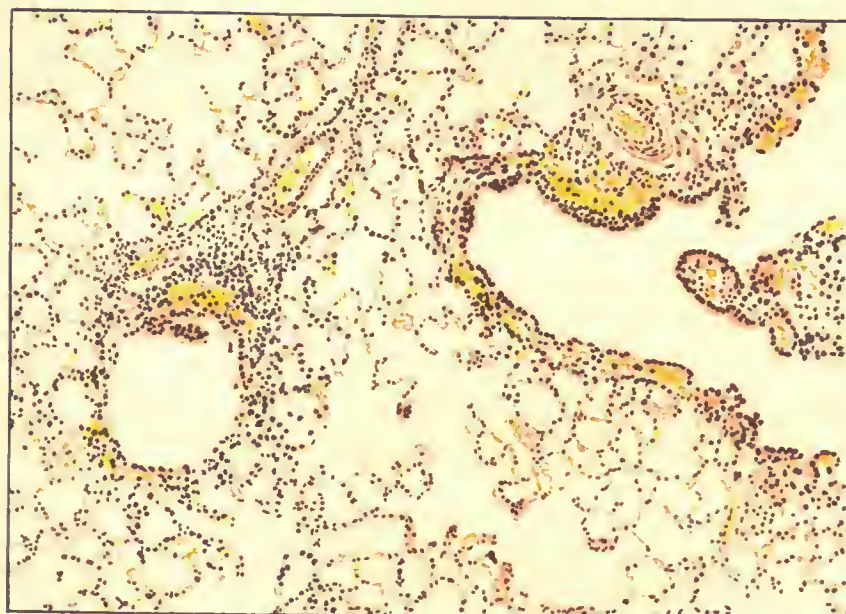


FIG. 77.—Lung of "recovered" dog killed four days after chloropierin gassing. In alveoli surrounding the bronchioles there are structures resembling giant cells. As shown in Figure 78, the structures are composed of fused mononuclear cells inclosing bits of old fibrin and degenerated red cells

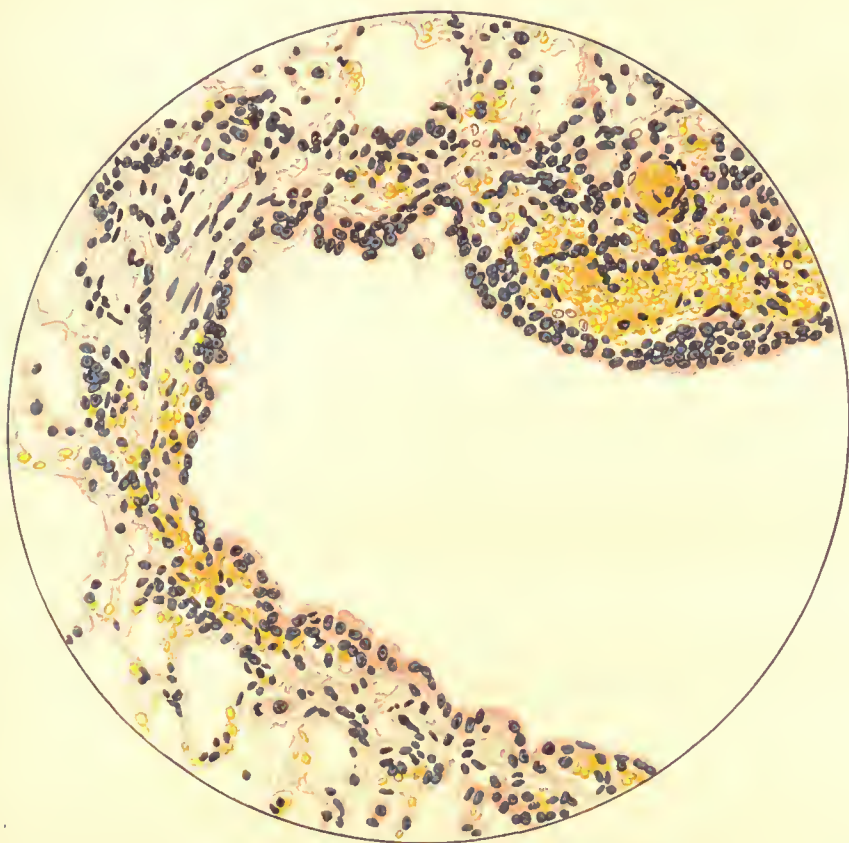
and medium-sized bronchi. Although the injury may have extended to the distal alveoli as well, causing focal areas of necrosis in the lung (see figs. 51 and 52) and desquamation of the alveolar epithelium, the most severe injury was suffered by the trachea and bronchi.

Phosgene, on the other hand, spared the trachea and larger bronchi, but destroyed the epithelial lining of the smaller bronchi and bronchioles. Even the outer coats of the smallest air tubes showed evidence of serious injury, and the alveolar walls were everywhere damaged though rarely necrotized.



A. REED & A. S.

MULTIPLE HEMORRHAGES IN WALL OF BRONCHUS OF DOG KILLED SIX DAYS
AFTER EXPOSURE TO CHLOROPICRIN.



A. MOEN & CO

HIGHER MAGNIFICATION OF BRONCHUS SHOWN IN PLATE XIII.

Note particularly the flattened character of the regenerating bronchial epithelium. A mitotic figure is seen on the left.

Chloropierin occupied an intermediary position in its action on the respiratory epithelium. The lining cells of the trachea and the very large bronchi were definitely injured in places, as shown by irregularities in the ciliated surface or loss of cilia and occasional desquamation of the superficial layer of cells. But there was nowhere seen the rapid and complete coagulation of the entire mucous surface such as chlorine produced. The medium-sized and smaller bronchi, on the other hand, suffered very severe damage, which was even more marked than with phosgene. There was often complete disintegration of the walls of the bronchioles. The changes in the alveolar walls were practically the same as those produced by phosgene.

This difference in the behavior of the three gases toward the several portions of the respiratory tract is not easily explained, but must be related in some way to the fact that chlorine required no preliminary decomposition for its action, thus hitting hardest the first tissues with which it came in contact; whereas phosgene, and probably chloropierin also, must be broken up, a process which may take place in the moist air of the smaller bronchi, or in the cytoplasm of the lining epithelium while being absorbed, or, as Hoover⁴ has suggested in the case of phosgene, only after absorption. The place and rate of absorption and decomposition would thus determine the site and degree of injury.

EDEMA AND CONGESTION

Each of the three gases produced a high grade of edema of the lungs, which developed with great rapidity after exposure. Its development was more rapid with chlorine and chloropierin than with phosgene, where corresponding toxic concentrations were used. In the two former a maximum degree

of edema was reached in less than 12 hours; whereas after phosgene the peak was reached in about 18 hours. But the time varied greatly with individual animals.

The actual quantity of fluid poured out into the lungs, as judged by the lung-heart and lung-body ratios, was slightly greater with phosgene than with chloropierin, although with the latter the fluid filled the lungs more completely (no figures are available for chlorine). This point will be taken up again in connection with the volume of the lungs. In both chlorine and chloropierin gassing there was a very striking edema of the mediastinal tissues and the pleura; this was not as conspicuous with phosgene.

Congestion of the lungs, although present in all, was much more pronounced with phosgene than with the other two gases, and constituted one of the distinguishing gross features. Phosgene lungs were almost regularly dark bluish red or purple, with whitish emphysematous patches; chloropierin lungs, on the other hand, as a rule, were lighter in color, the basic hue being a bluish pink.

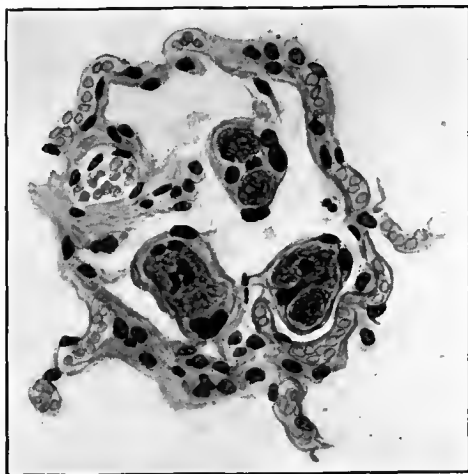


FIG. 78.—Higher magnification of an alveolus from Figure 77, showing the structure of phagocytic giant cells. Note their resemblance to capillaries

EMPHYSEMA AND RESIDUAL AIR

The development of focal emphysema was seen with all three gases, but phosgene easily ranked first in the number and extent of the acutely distended foci of lung tissue. A comparison of the illustrations of gross lesions emphasizes the differences. Figures on the weights and volume of chloropierin and phosgene lungs supply more exact data, particularly as regards the total amount of residual air.

In 18 phosgene dogs dying within 24 hours after gassing, the average volume of the lungs was 579 c. c.; weight 459 grams. In 30 chloropierin animals the figures were 413 c. c. and 353 grams. The average weight of the dogs in the two series was approximately the same, 12 kilos. Phosgene lungs were seen to be greater in both volume and weight, but the difference between the average weight and volume, which represented roughly the amount of residual air confined chiefly in emphysematous patches, was 129 in the phosgene series, while in the chloropierin series it was less than half this amount (see Table 57 for chloropierin figures). The contrast in the gross appearance of the lungs was often much more striking than these figures would suggest. In many instances the chloropierin lungs were uniformly doughy and airless, and the figures of the weight and volume were practically the same, or differed by only 10 to 25 points. With phosgene no such close approximation of the weight and volume was observed, the smallest difference noted being 50, this being in a small dog, weighing only 5.5 kilos, where the volume of the lung was 325 c. c. and weight 275 grams.

RESPIRATORY INFECTION AND CHRONIC CHANGES IN THE LUNGS

An inflammatory reaction was seen in the lungs of almost every animal that died more than 24 hours after gassing with chlorine, phosgene, or chloropierin, and in a large proportion of those dying earlier. In this particular, there was practically no difference in the three gases. But the percentage of animals which succumbed to the infection after passing through the acute edema stage appeared to be somewhat higher with chlorine than with the other two gases. The secondary rise in the death curve (see Chart XXIV) shows this to be so. In view of the greater injury to the trachea and bronchi produced by chlorine, which allowed not only the freer entry of pathogenic bacteria into the lungs, but also led to a necrotizing tracheitis and bronchitis as well, the particularly large number of delayed deaths from infection was not surprising. As might be expected, chloropierin came second to chlorine in producing a condition favorable to infection. Indeed, in the matter of infections of the pleural cavity—fibrinous pleurisy and empyema—it appeared to stand first, but the series of cases was small, and the percentages were therefore less conclusive.

The late changes in the lungs—that is, the lesions found in animals which had died or had been killed ten days to several months after gassing—were practically the same for all three gases; focal emphysema and atelectasis, chronic bronchitis, generally of the obliterative type, and occasional examples of bronchiectasis. An active chronic infection in and about the bronchi, with patches of organizing pneumonia, was seen not infrequently. On the whole these chronic changes were most pronounced after chlorine gassing, but the character of the lesions was the same in all, and similar pictures have been described for other gases of the respiratory irritant group.

In other words, it was only in the acute period that it was possible to distinguish between the effects of these gases, and even then it could be done only by an experienced observer who was familiar with the variations in the lesions produced by each gas.

SUMMARY

A comparative study of the pathology of chloropicrin, chlorine, and phosgene shows that chloropicrin in its action on the respiratory tract, occupied an intermediate position between chlorine and phosgene. It damaged the trachea and larger bronchi less than chlorine, but more than phosgene. In its action on the bronchioles and alveoli, it resembled phosgene very closely, and in several other respects the lesions were more like those of chlorine. The gross and microscopic differences in the acute effects of the three gases on dogs were sufficiently clear to enable an experienced observer to determine by autopsy which gas had been used. It should be possible to make practical application of this knowledge on the battlefield in the identification of the gas being used by the enemy.

CYANOGEN COMPOUNDS

The experimental pathology of three compounds of this group, hydrocyanic acid, cyanogen chloride, and cyanogen bromide, was investigated at the American University laboratories by Winternitz, Finney, and Wislocki.¹³ The following is a summary of their report.

The rapid and fatal action of hydrocyanic acid and certain of its salts was referable to its property of interfering with tissue oxidation, so that, as Geppert¹⁴ stated many years ago, "there is an internal suffocation of the organs." The involvement of vital centers in the central nervous system accounted for the sudden death when a lethal dose was administered. It was not surprising that with such rapid action, little or no distinctive anatomical change should be produced. The blood was bright red, and coagulation was delayed, resulting in a scarlet instead of the usual bluish lividity in the dependent parts. If potassium cyanide reached the stomach undecomposed, it formed, with the hemoglobin, a striking red or blue cyanmethemoglobin compound. The mucous membrane was soapy, slippery, covered with blood-tinged mucus, and quite transparent at the crests of the folds. This change was brought about by the alkaline action of the potassium, and was regarded as characteristic. It was claimed by Kobert¹⁵ that increased pressure in the ventricles of the brain might occur in the more delayed action of the poisoning. The right heart was usually distended, the left empty. Post-mortem digestion set in rapidly, especially in the liver. The lungs might be edematous, and the urine might contain blood and sugar.

With hydrocyanic acid there was no essential delayed action, and experimental results (Marshall¹⁶) indicate that if an animal did not succumb during exposure to the gas, it recovered, and there were no anatomical changes found when the animal was sacrificed. It follows, therefore, that changes which occurred in animals subjected to chlorine and bromine compounds of cyanogen were probably, in large part at least, the result of the action of the halogen radicals.

CYANOGEN CHLORIDE

The action of this gas was similar to that of hydrocyanic acid in that a lethal exposure resulted in death within a few minutes, apparently from paralysis of the respiratory center. Marshall and Miller,¹⁶ in a large series of experiments, observed no delayed deaths, and they stated that if an animal survived 15 to 20 minutes after removal from the gas chamber it would recover. In this respect the gas differed quite strikingly from chlorine, phosgene, and chloropicrin, which did not cause immediate death except in extremely high concentrations.

The anatomical changes in cyanogen chloride poisoning were studied in two groups of dogs: (1) Those that succumbed during or immediately after exposure, and (2) recovered animals killed at varying intervals up to two months after gassing. The former showed a moderate degree of pulmonary edema and congestion, associated with an early inflammatory reaction in the bronchioles. The edema was inconspicuous with minimal lethal doses, but it was definitely augmented as the concentration of the gas was increased. The recovered animals showed a catarrhal bronchiolitis associated with slight localized vesicular emphysema and atelectasis, and rarely, small foci of bronchopneumonia.

These findings show that in addition to a cyanogen action, there was a definite, though mild, injury to the respiratory tract, which was undoubtedly referable to the halogen radical.

CYANOGEN BROMIDE

The action of this gas was somewhat different from that of the chlorine derivative. While animals might succumb suddenly from short exposure, death some hours or even several days after exposure was more common.

The lesions in acutely fatal cases (death within 24 hours) resembled closely those caused by chlorine. The entire respiratory apparatus suffered, particularly the trachea and bronchi. The lung showed the same picture of extreme edema and congestion as was seen in gassing by other respiratory irritants.

Animals dying after 48 hours generally showed well-marked respiratory infection; tracheitis, bronchitis, and bronchopneumonia, associated with more or less edema and congestion. As in the more acute deaths, the changes found were practically indistinguishable from those caused by chlorine.^h The marked involvement of the upper respiratory tract differentiated the condition from phosgene poisoning.

Animals which recovered from a fairly severe exposure showed quite regularly residual lesions in the lungs of the nature of a chronic bronchiolitis, organizing or suppurative with more or less emphysema (Fig. 79).

ARSINE (AsH_3)

The chemical properties and physiological action of arsine have been discussed elsewhere. Since, however, the anatomical changes produced by lethal exposures to the gas are intimately related to the action of the poison on the blood, it may be well to restate in this connection the salient facts regarding this action. Arsine is absorbed through the lungs and passes into the blood

^h Microscopic sections of the organs of these animals have not been examined. It would be interesting to see whether the lungs show focal hyaline necroses of the septa such as are found in fatal chlorine gassing.

stream apparently unchanged. There it enters into combination with the hemoglobin of the erythrocytes, forming a compound which gives a brownish color to the blood. After several hours, the affected blood cells rupture (hemolysis), setting free hemoglobin, which is excreted by the kidneys, appearing in the urine both as methemoglobin and oxyhemoglobin, and by the liver which converts it into bile. An excess of free hemoglobin is found in the blood and is absorbed by many of the tissues, particularly those in direct contact with the blood stream, such as the intima of blood vessels. It is important to note that this striking hemolytic action is dependent on the presence of oxygen or some

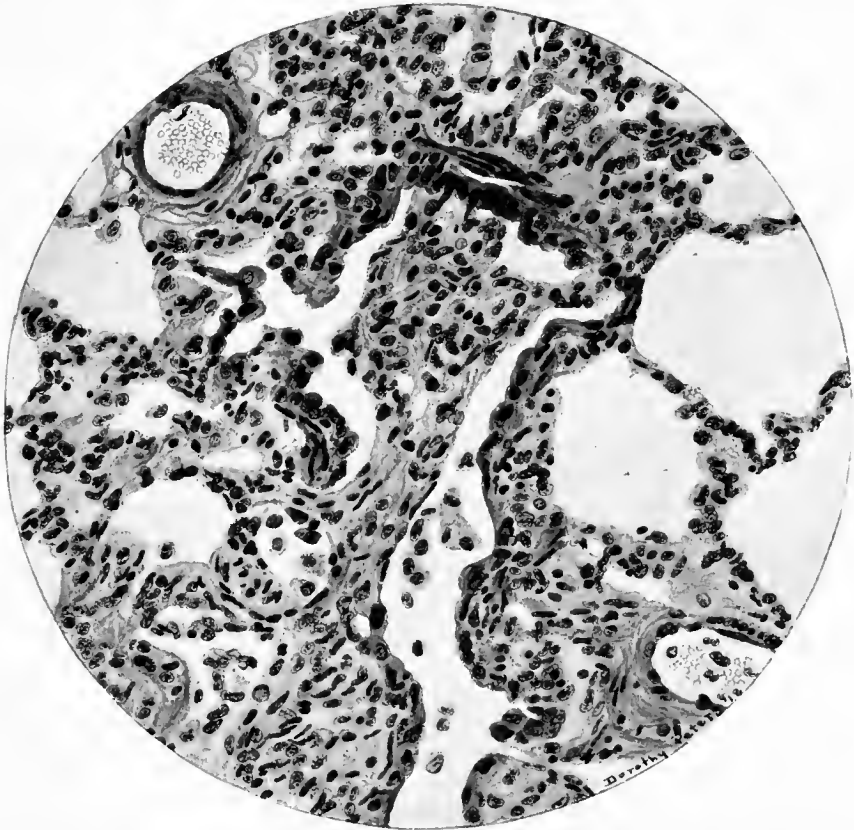


FIG. 79.—Organizing bronchiolitis in a dog killed two months after exposure to cyanogen bromide. The character of the cells taking part in the organization is well shown. The bronchiole has been partially relined by an epithelium of irregular form but mostly of the flattened type

oxidizing substance, and that a period of several hours is necessary for the completion of the reaction. This latent period has been observed both in vivo (prejaundiced stage) and in vitro.

As might be expected, one of the most serious effects of such a hemolytic agent is the rapid development of an anemia of severe grade. The blood changes in a dog receiving a sublethal exposure are shown very strikingly in the rapid fall in the number of red blood cells, with a gradual restoration to normal as the animal recovered. There was an associated leucocytosis, pre-

sumably a toxic reaction. Wislocki¹⁷ states that the hemoglobin in severe cases may fall to 20 per cent or even lower, and that the erythrocyte count not uncommonly sinks to one or two million within 72 hours. Blood films show basophilic stippling, poikilocytosis, and anisocytosis. The appearance in the circulation of numerous normoblasts and occasional megaloblasts indicates an active attempt at regeneration on the part of the bone marrow.

GROSS FINDINGS

The following summary of the pathological anatomy of arsine poisoning is taken from Mackenzie's¹⁸ report of observations at the American University.

Arsine produced a pathological picture which had practically nothing in common with the changes characterizing the gases known as lung irritants. Locally, there was no irritant action, animals showing no distress during exposure; nor did the bronchi or lungs, through which the gas was readily absorbed, show any anatomical changes suggesting that there was direct action upon any of the tissues of the respiratory system. As a rule the lungs were grossly quite normal in appearance, except for areas of atelectasis at the bases and along the margins of the lower lobes. These, like the small amount of edema in the alveoli, seen in microscopic sections, and the occasional appearance of effusions in the pleural cavities, probably appeared just before death, coincident with failure of the circulation and extreme oxygen want. It was upon the blood, and particularly upon the red blood cells, that the chief action of arsine was exerted.

At autopsy, the skin, mucous membranes, intima of blood vessels, and the serous layer of the gut were stained a dusky red color. This staining of the tissues obscured somewhat the jaundice which was constantly present. In the sclerae, liver, and fatty tissues, however, it was very apparent. The post-mortem clots in the heart had a uniform, almost black, appearance without any of the chicken-fat quality. The liver was swollen and jaundiced and the gall-bladder full of dark, viscid bile. The enormous production of bile was shown by the presence of large amounts throughout the whole alimentary tract from the esophagus to the rectum. The spleen was enlarged and soft; often its anterior tip extended to the midline of the abdomen. It was deep bluish in color, and on section the pulp was dark, soft and smeary; the follicles indistinct or invisible. In addition to the staining of the serosa and the abnormally large amount of bile, the intestines sometimes showed blood-stained contents. No ulcerations or other gross lesions, however, were seen. Pancreas and adrenals showed only the dusky red discoloration.

The kidneys presented a remarkable appearance. They were swollen and soft. The capsule stripped off easily, leaving a smooth surface which, in the more severe poisonings, was almost black in color. When the action was less intense, the surface showed scattered patches of blue-black color on a background of deep red. On section the cortex was wide and bulging, and the striations, though less distinct than in a normal kidney, were regular and straight. Both cortical and pyramidal portions showed the dark blue-black discoloration. The bladder contained brownish black urine, which, in thin layers, had a reddish tinge. In the bladder there was also found a precipitate of black amorphous material which yielded a strongly positive test for arsenic; a watery extract of it gave the spectrum of methemoglobin. The bone marrow was dark, grayish-red, and firm.

MICROSCOPIC APPEARANCES

Lung.—A small amount of coagulated fluid was found in the alveoli. This was probably not the result of irritant action by the gas, but merely a terminal event, comparable to the pulmonary edema so frequently found at autopsy in cases of pernicious anemia.

Heart.—Nothing more than pallor of the muscle fibers was found.

Liver.—The liver cells were swollen and frequently contained an abnormal quantity of fat. In the bile canaliculi and in the lymphatics of the portal spaces dark greenish-brown droplets of bile were seen.

Spleen.—The follicles were large, but the cells seemed less closely crowded together than normally. The pulp contained relatively few cells. It was filled with formless material, staining, in hematoxylin and eosin preparations, a pale pink or pale greenish-yellow color. Evidently this material was hemolyzed blood and the debris of laked corpuscles. A few nucleated red cells and plasma cells were found in the pulp and a scattering of large mononuclear phagocytes frequently laden with pigment. The histological picture gave the impression that the splenic enlargement was due to the filter action of the pulp removing from the circulation the fragments of destroyed corpuscles.

Stomach, intestines, pancreas, and adrenals.—Nothing abnormal. Degeneration of the cells of the adrenal medulla, described for poisoning by other arsenic compounds, was not seen.

Kidneys.—The capsular spaces and lumen of the tubules were filled with hemolyzed blood and often, also, hemoglobin crystals. Sometimes one saw the straight tubules apparently plugged by a mass of crystals. In the cytoplasm of the epithelial cells lining the straight tubules, and to a less extent in the epithelium of the convoluted tubules, accumulations of small dark-brown crystals were frequently found. In two of the animals was seen degeneration of the epithelium lining the convoluted tubules. It is quite possible that this was the result of obstruction by crystals in the collecting tubule. One dog, which survived the gassing nine days, showed evidences of epithelial regeneration. The process in the kidney, therefore, appeared to be as follows: Free hemoglobin or a combination of hemoglobin and arsenic was removed from the circulation by the glomeruli and tubules. If the concentration of hemoglobin was sufficiently high, crystallization took place, and the crystals, becoming impacted in the lumen of the collecting tubules, caused obstruction. This resulted in a rise of pressure within the obstructed tubule and consequent degeneration of the epithelium. The gross discoloration of the kidneys was due in part to the deposition of crystals in the cytoplasm of the kidney cells, but chiefly to the filling of the tubules with methemoglobin, and the vessels of the kidney with the brown product of hemolysis by arsenic oxide. An obvious therapeutic indication from these findings is the administration of large amounts of fluid in order to keep the concentration of hemoglobin in the kidney at the lowest possible point.

Bone marrow.—There was no evidence of any direct action on the marrow. With the development of anemia, however, the stimulus of oxygen want caused a striking hyperplasia of the marrow. The increased activity was shown by myeloblastic as well as erythroblastic cells.

The following case illustrates very well the effects of arsine on the blood cells. Dog exposed 30 minutes; concentration 0.53 mgm. per liter. Six

hours after gassing there was hematuria, which continued four days. Other symptoms were diarrhea, tarry stools, marked weakness, and depression. Eventually recovery was complete. Table 58 shows the quantitative changes in red blood cells and leucocytes. Note the rapid fall in erythrocytes, which reached their lowest figure on the fifth day, after which there was a gradual restoration to normal. There was at first a fall in the leucocytes, then a marked rise, and finally a gradual decline. Normoblasts and megaloblasts appeared in the circulation in the period of active regeneration.

TABLE 58.—*Blood changes following gassing with arsine*

	Erythrocytes	Leucocytes	Small lymphocytes	Large lymphocytes	Large mononuclears	Transitionals	Poly-morpho-nuclear neutrophils	Eosinophiles
Before gassing.....	6,530,000	22,400	4	6	2	1	69	17
Time of gassing.....	5,800,000	20,200	4	6	1	2	60	27
6 hours after gassing.....	3,480,000	12,800	4	6	0	2	80	8
First day.....	2,660,000	23,200	4	3	0	1	88	4
Second day.....	2,450,000	25,400	5	0	0	0	93	2
Third day.....	2,300,000	70,000	1	0	0	0	99	0
Fourth day.....	2,250,000	66,500	6	2	0	1	90	0
Fifth day.....	2,570,000	54,800	4	1	0	3	92	0
Tenth day.....	3,750,000	15,600	11	17	2	4	85	4
Fifteenth day.....	4,060,000	15,800	8	8	1	0	74	6
Twenty-fourth day.....	5,010,000	14,800	10	10	3	2	51	24

RECOVERED ANIMALS

Wislocki ¹⁷ makes the following note on pathological changes in animals which survive "lethal" exposure and are killed after partial or complete recovery.

After four to six days the jaundice, which is so characteristic of the second stage, fades. The hemoglobinuria ceases; the viscera lose their icteric tint, but for some time possess an abnormal pallor, attributable to the anemia from loss of blood.

The red cell counts and hemoglobin estimations gradually rise. Evidence of the stimulation of the hemopoietic function is seen in the presence of immature erythroblasts in the peripheral circulation. Microscopically, the bone marrow is found slightly hyperplastic, showing numerous erythroblasts in all stages of development.

Liver and spleen show no trace of their former condition beyond, under the microscope, the presence of pigment granules in mononuclear phagocytes.

The kidneys do not appear to have been severely damaged, for every trace of the methemoglobin disappears, and the injured tubules are restored to normal. Deposits of hemosiderin are encountered for some time.

SUMMARY

The pathological changes found in arsine poisoning were referable directly or indirectly to the lytic action of the gas on the red blood-cells. An acute anemia resulted, with a staining of the tissues by the freed hemoglobin. Jaundice developed rapidly.

Microscopically, methemoglobin was found in amorphous and crystalline form in the lumina of the kidney tubules and in the renal epithelium. Bile pigments were deposited in practically all organs and tissues.

In recovered animals there was active and rapid regeneration of the blood, with bone marrow hyperlasia. The blood pigments were gradually removed from the tissue apparently by phagocytosis.

ORGANIC COMPOUNDS OF ARSENIC

The number of toxic organic compounds of arsenic is quite large, as pointed out in the discussion of the chemistry of this group of substances. But relatively few organic arsenicals were utilized in the World War. Diphenylchlorarsine, diphenylecyanarsine, and chlormethylarsine are mentioned by Clark and Pappenheimer¹⁹ as being those most employed.

Diphenylchlorarsine and diphenylecyanarsine are solids which in finely divided form produce an extremely irritating and penetrating smoke, causing sneezing and lacrymation (blue cross shells). Bromomethylarsine and chlormethylarsine are liquids which in vaporized form injure the respiratory tract, eyes, and skin in very much the same way as does mustard gas.

In addition to these four compounds, a number of closely related substances including ethyl-, methyl-, and phenyldichlorarsine, ethylarsine, methyl-diiodoarsine, cacodylcyanide and chloride, diphenyliodoarsine, and diphenylarsine oxide were investigated in the American University laboratories, but thorough anatomical and histological studies were made only in the case of methyl-, ethyl-, and phenyldichlorarsine. Preliminary studies, however, with various members of the group, indicated that while they might vary considerably in toxicity, the lesions produced by lethal exposures were essentially the same in all.

Investigations carried out by Dunn²⁰ for the medical research committee of the British Army Medical Service also showed that the effects of the several arsenicals studied, diphenylchlorarsine, diphenylarsenious oxide, and phenylarsenious oxide, are identical, and that the effect produced in different species of animals (goats, dogs, guinea pigs, cats, monkeys, and rabbits) are much the same.

METHYL-, ETHYL-, AND PHENYLDICHLORARSINE

These compounds were very thoroughly investigated at the American University. Dogs were subjected to various concentrations of each of the vaporized substances in a gassing chamber. As with other toxic gases studied, it was found that a certain percentage of the exposed animals died shortly after gassing, whereas some succumbed only after several days, and others completely recovered. The numbers falling into each of these groups, particularly the acute deaths and recoveries, varied, as might be expected, with the degree of concentration of the gas and the length of exposure. The lesions associated with death in the first stage, that is within the first two days, were most distinctive of the gas injury, since in the later deaths, the gross and microscopic picture in the respiratory tract, where the damage was greatest, was regularly obscured by the reaction to a superimposed infection. The lesions produced by the three compounds differed in degree rather than in kind and may therefore be discussed together.

The following summary of Finney's observations²¹ on the effects of methyldichlorarsine will serve as a basis for all.

ACUTE DEATHS

After exposure to high concentrations, death might occur within 4 hours, but rarely occurred before 18 to 24 hours. While in the gassing chamber the dogs showed signs of marked irritation and often became excited. There was profuse lacrymation, salivation, and nasal discharge, accompanied by sneezing and

often by retching and vomiting. After removal from the chamber, the animals were depressed, had no appetite, and began to exhibit more or less respiratory distress. Vomiting was frequent and diarrhea might be present. After a few hours, wheezing and râles might be heard, and the rate of respiration was increased. The pulse became rapid and feeble as the respiratory signs were augmented, and the animal became semicomatose and died in collapse. The pathological findings in these acute animals were as follows:

The conjunctivæ were reddened and congested; there was often a frothy discharge from nose and mouth; the skin of the groins where sparsely covered by hair frequently showed red patches, extending throughout the thickness of the corium.

On opening the thorax, the lungs were voluminous, nearly filling the chest. All lobes usually shared equally in the increase in size and other changes. The pleural surfaces were moist, without the presence of free fluid in the pleural cavities. The surfaces were smooth, bright red in color, with more or less mottling over the surfaces, caused by alternating groups of air-containing and serum-containing alveoli. On removal, the lungs were felt to be heavy and the lobes retained their shape well, although hanging in a sodden mass from the hilus. On section, the cut surfaces dripped frothy pink fluid mixed with blood. The color was not uniform, but areas of darker red appeared here and there throughout the lungs. These areas were often firmer in consistency than the more normal spongy tissue, and gave the impression of jelly which had begun to set. The anterior tips of the middle and upper lobes most frequently showed these dark red areas.

The bronchi were usually not conspicuous on the cut surface of the lung, though they were sometimes filled with tenacious fibrinous plugs. The trachea, however, showed a striking false membrane throughout its entire length. The membrane was quite thick and edematous, sometimes quite white in color, in contrast to the walls of the trachea, which were congested and often intensely red. More frequently the membrane was stained pink by the frothy fluid which poured up from the lungs. In the earliest stages, the membrane could usually be stripped entire from the surface beneath; later on it lost its tough elastic quality, became yellowish, softer, heavier, and finally, purulent and necrotic. The surface beneath was red and raw, and occasionally small bleeding points could be seen. The larynx, up to the vocal cords, showed, a continuation of the membrane; above this point, the congestion and edema of the mucosa was still present, but the membrane was lacking. The formation of this membrane took place quickly and was found in dogs dying as early as four hours after exposure. In many of these extremely acute dogs there was no membrane but, instead, congestion and some edema of the mucosa. In dogs dying at the end of the second day or later the membrane was replaced by thick, purulent exudate.

The heart was dilated and filled with dark red, almost black, post-mortem clot, particularly on the right side. The pericardial fluid was not increased in amount and was not bloody.

The abdominal viscera might show moderate degrees of congestion, but this was never a striking feature. The liver was firm and dark red. The spleen varied considerably and was usually slightly swollen, presenting a smooth, soft surface; on section its Malpighian bodies were not conspicuous. The

kidneys presented a smooth surface, a dark red cortex, with usually a lighter pyramid, and no marked abnormalities. The adrenals looked entirely normal on the surface; but on section, the medulla was usually markedly congested and occasionally pin-point hemorrhages could be seen at the line of juncture of cortex and medulla. The intestines showed nothing of especial interest; the mucous surfaces were not congested. The urine found in the bladder had its normal yellow color.

Microscopically the only changes of importance were in the respiratory tract. The membrane in the trachea was found to consist of a fibrin network with large spaces full of edematous fluid. The epithelial lining of the trachea had been lifted off and in some cases could be seen as a ragged line floating out through the edematous fibrin. In the early stages, there was but little polymorphonuclear infiltration; but this became more marked in a short time, and the membrane might stain a dusky purple, because of the presence of pyknotic nuclei of leucocytes. The submucosa also showed some leucocytic infiltration, but this never became extreme, and many of the leucocytes were mononuclear; the edema of the submucosa was also of a moderate degree. Sometimes the inflammatory process extended beyond the cartilaginous rings. Later on the membrane became a dense mass of necrotic purple-staining material, which lay upon the submucosa, with no intervening epithelial layer. It was noticed in many cases that while the epithelium was completely denuded over the greater part of the circumference of the trachea, it was still intact over the posterior portion; that part which was not surrounded by cartilage.

In the lungs the microscopic changes were principally those associated with the congestion and edema seen in the gross. The edema was rarely of even distribution throughout the section, but groups of alveoli were seen filled with pink-staining homogeneous material adjacent to other groups of alveoli over-distended with air. (Fig. 80.) This corresponded to the mottled appearance presented by the surfaces of the lungs. The capillaries of the alveolar walls, particularly in the edematous areas, were tortuous and filled with red blood cells. The alveolar epithelium seemed to have suffered little, and was in most places intact; where edema was most marked, there was more or less desquamation and swollen round cells were found floating in the fluid. In places much fibrin could be seen in the edematous alveoli. The bronchi showed a continuation of the tracheal membrane (fig. 81), but the bronchioles usually presented an intact epithelium. Frequently there was marked peribronchial and perivascular edema. (Fig. 82.)

Microscopic changes in the other organs were of minor degree, and consisted of slight swelling and granulation of cells in the liver and kidneys, and of congestion of the vessels of the adrenal medulla with occasional minute hemorrhages.

DELAYED DEATHS

The dogs of this group showed more variation than those of the first group. Those which died in two or three days showed a persistence of the acute conditions described above, upon which was superimposed a beginning pneumonia. Those which died toward the end of the two-week period showed little trace of the original conditions, but had extensive pneumonia of various types.

It appeared from a study of the microscopical sections that the pneumonia could develop in two ways. First, the extensive edema of the acute

stage might become diffusely infiltrated with polymorphonuclear leucocytes, and the edema might change to a cellular exudate over large areas of lung, bearing little direct anatomical relationship to the bronchi. Second, the smaller bronchi and bronchioles could become ringed with leucocytes, their epithelium degenerated, their walls infiltrated, and each bronchiole the center of a small focus or nodule of pneumonic consolidation.

In the first case the consolidated area may have occupied all of a lobe or several lobes, and the lungs may have retained a heavy, wet consistency. In the second case the areas involved were practically always the anterior tips of the middle and upper lobes, while the posterior portions of these lobes and the whole of the lower lobes presented an air-containing and emphysematous condition, sometimes with slight congestion, sometimes with none.

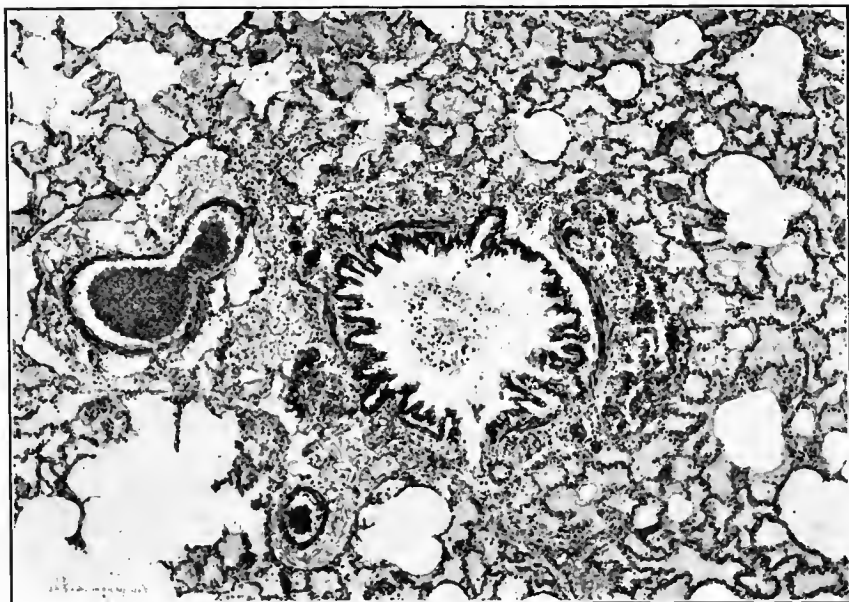


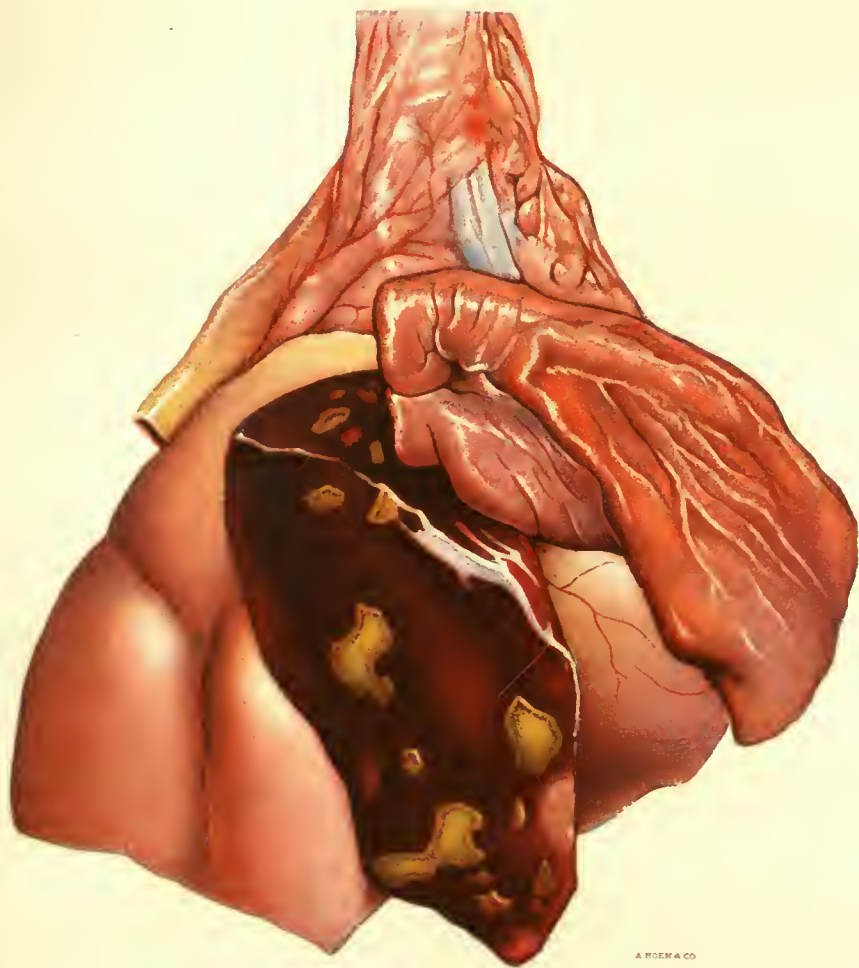
FIG. 80.—Widespread edema of lung in acute death from dichlorethylarsine. The clear round spaces indicate the presence of air bubbles

The pneumonias were of different types: Some were soft, wet, and purulent, with the bronchi containing streams of purulent material; others were firm, gray, solid pneumonia; still others were red, with many small discrete gray nodules standing out on the cut surface.

In dogs which lived for some time after the development of pneumonia, abscesses were occasionally found, with fibrinopurulent pleurisy. (Plate XV.) The acute conjunctivitis of the early stage subsided and rarely developed into a purulent discharge. Ulceration of the cornea was found in only one or two isolated cases. (Fig. 83.) The skin lesions also subsided without ulceration, blistering, or sloughing.

RECOVERED ANIMALS

Some dogs which survived for three weeks or more after exposure died with acute pneumonia of only a few days' duration. Others died with extensive purulent pleurisy or empyema. There seemed to be no definite proof that



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PNEUMONIA COMPLICATED BY MULTIPLE ABSCESS FORMATION AND PLEURISY
FIVE DAYS AFTER EXPOSURE TO DICHLORETHYLARSINE.
Only one lobe is consolidated; others are relatively emphysematous.

these animals developed this condition as a result of exposure to the gas, as some animals came to autopsy with the same lesions before exposure to any gas.

Those dogs which survived for long periods and were sacrificed for autopsy showed no gross anatomical lesions. Microscopically, no changes were found in the lungs or bronchioles (in the trachea there was sometimes evidence that the epithelium had not recovered its normal thickness or structure).

DISCUSSION

From the above description it is clear that methylchlorarsine produced an escharotic action on the tubular portion of the respiratory tract, including larynx, trachea, and the main bronchi, and that there was marked though less

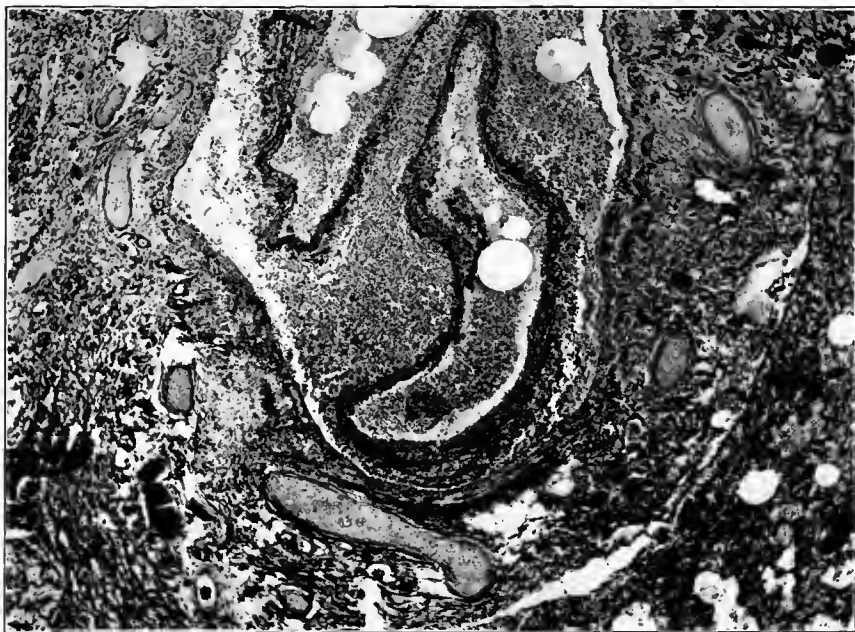


FIG. 81.—Necrotization of the bronchial lining associated with acute death from dichlorethylarsine. A few air bubbles are seen in the exudate filling the lumen

severe damage to the branches of the bronchial tree and the alveolar walls. The resulting lesions were a membranous laryngitis (figs. 84 and 85), tracheitis and bronchitis (fig. 86), edema and congestion of the lungs. The smaller bronchi were often plugged by masses of exfoliated epithelium dislodged downwards from trachea and large bronchi. A focal emphysema and atelectasis were found as secondary phenomena, and hemorrhages into both alveoli and interstitial tissue about the blood vessels and bronchi at times constituted an added striking feature. Small hemorrhages were much less commonly found in the adrenal and liver.

Among the animals which survived the acute period, a certain number, as indicated above, died after 2 to 10 days or even longer. In practically all of these, the chief cause of death was found to be a widespread infection of the respiratory tract, generally a suppurative bronchitis and bronchopneumonia;

abscess formation and more rarely a suppurative pleurisy were present occasionally. In other words, the picture was not different from that associated with similar delayed deaths after mustard or chlorine gassing. Finney's studies of recovered animals killed considerable periods after gassing with methylchlorarsine showed neither grossly nor microscopically any chronic or healed lesions.²¹ The significance of this observation is discussed on pages 483, 508 in connection with the residual lesions of the various gases of the respiratory irritant group.

The effects of ethyldichlorarsine and phenyldichlorarsine Finney found, in general, to be practically the same as those produced by the methyl compound just described. A few minor differences were noted. For example, the ethyl compound seemed to be more potent in the production of hemorrhages than

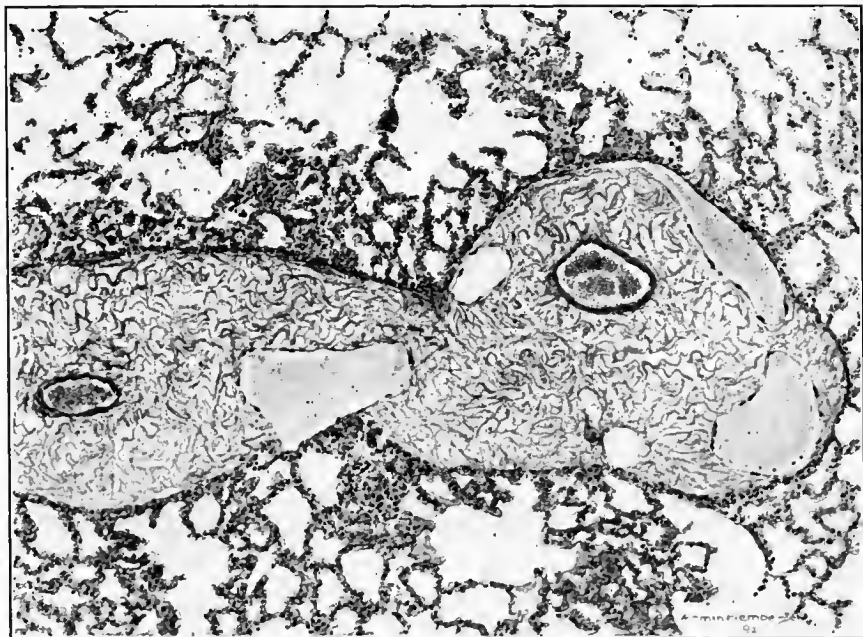


FIG. 82.—Marked perivascular edema and dilatation of lymphatics in acute dichlorethylarsine gassing

the other two, whereas phenyldichlorarsine produced the most severe tracheal injury. It is questionable, however, if even these minor points of difference may not be referable to differences in toxicity.

A comparison of the effects of these organic arsenic compounds with gases more widely used in the war—chlorine, phosgene, chloropierin, and mustard—shows that the lesions of the former most closely resembled those produced by mustard gas. Indeed, it would have been quite difficult, either grossly or microscopically, to distinguish the tracheal lesions in the two cases. Finney pointed out, however, that the organic arsenicals of this group did not damage the distal portion of the bronchial tree, as mustard gas did, and that the eye effects were different. The arsenicals produced an acute irritation of the eyes, with much discomfort, as evidenced by the behavior of the animals, but the injury was slight and the conjunctival reaction transient. Mustard gas, on the other hand, caused much less irritation—that is, subjective disturbance—but far more serious damage to the ocular tissues.

With arsine (AsH_3) which acts primarily as a blood destroyer or hemolytic agent, the group of organic arsenicals apparently has nothing in common from the standpoint of anatomical effect. It is also noteworthy that injury to the kidney, such as Pearce and Brown²² found, was produced by a number of the organic arsenicals which they tested, was not observed in dogs gassed by any of the four compounds discussed here, although owing to the different mode of administration (subcutaneous and intravenous in the one and pulmonary in the other) the tests are perhaps not properly comparable.

It would appear, therefore, that the toxic property in methyl-, ethyl-, and phenyldichlorarsine, as in mustard gas, is linked up with the chlorine radical, rather than the arsenical group. Certainly the changes in the tissues give support to this view.

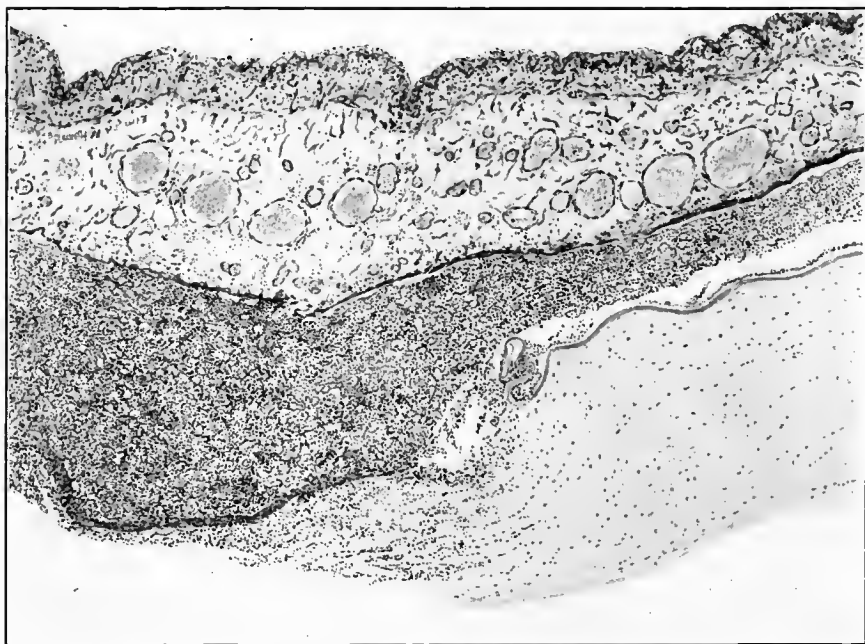


FIG. 83.—Ulceration of cornea following exposure to dichlorethylarsine. Perforation of the cornea has taken place with infection of the anterior chamber

DISCUSSION OF SOME OF THE PHENOMENA OF GASSING BY THE PULMONARY IRRITANT GROUP OF GASES

It is obvious from the detailed description of the pathological changes produced by toxic exposure to the various pulmonary irritant gases, that certain phenomena—pulmonary edema, circulatory disturbances, focal emphysema and atelectasis, complicating respiratory infection and hemorrhages, and residual lesions in recovered animals—were common to all. These changes have already been fully described. What is proposed here is simply the discussion of the significance of some of these phenomena from the anatomical standpoint.

PULMONARY EDEMA

Two phases of the question of pulmonary edema merit discussion: (1) The cause and mechanism of production; (2) the importance of the condition as a cause of death after gassing.

In respect to the cause of the edema, Edkins and Tweedy,² in a very thorough discussion of this fundamental question, set down the following main possibilities:

(1) It may be simply a response of increased lymph production to some appropriate local stimulation.

(2) It may be the result of damage to the alveolar epithelium and the capillary walls, such that increased permeability occurs as far as the plasma and its constituents are concerned, though not permitting diapedesis of erythrocytes. In severe poisoning, however, this may even occur.

(3) The damage done to the alveolar walls may lead to the formation of new chemical substances which osmotically induce a passage of water from the capillaries. It is perhaps even possible that the irritant substances themselves, or their chemical products, may be of minor importance in this respect.



FIG. 84.—Blister formation in epiglottis in a dog dying acutely from exposure to dichlorethylarsine. The epidermis is severely damaged and there is a widespread inflammatory reaction in the tissues beneath

(4) It may be the result of such disorganization of the walls of the vessels or spaces containing lymph that definite leakage is established.

These investigators mentioned also the possibility of defective lymphatic drainage as an important factor. The problem may be stated in somewhat simpler terms. Is the fluid a mere transudate which pours out through walls made pervious by direct injury or through disturbed circulation? Or does its coagulation represent a true inflammatory reaction comparable to that seen in the skin or other solid tissues, resulting from bacterial or chemical injuries? The inclination was to accept the latter view, namely, that the edema is a part of an inflammatory reaction and therefore essentially purposeful, although it seems impossible to exclude purely mechanical factors. Certainly the alveolar epithelium is damaged, and possibly also the adjacent capillary wall, though this is not readily demonstrable. But an injury that

would permit such a free outflow of fluid might be expected also to allow the exodus of red blood cells, whereas the active diapedesis of red corpuscles is exceptional. Furthermore, the presence of fluid in the interstitial tissue of the mediastinum and tracheal walls is more easily explained on an inflammatory basis. In supporting the idea of the inflammatory nature of the edema, it is granted that the mechanism of such a reaction is by no means settled. It would be of interest to review this problem here, but it would take one too far afield.ⁱ It may be added that there is accord with the views of Edkins and Tweedy, as expressed in the following paragraph:²

We are further led to the view that the edema is a consequence of excessive lymph production and that this production is the adapted response which the lung makes to the stimulus afforded by the irritant gas, or the changes in the tissues such irritant gases imme-



FIG. 85.—A higher magnification of one of the blisters shown in Figure 84. The fluid of the bleb is rich in fibrin which stains deeply

diately induce. The accumulation, though its advantage in maintaining or restoring the lung tissue may be great, has the disadvantage that it may fatally interfere with the gaseous exchange. However necessary its appearance may be to combat the poison, when in excess, it is as desirable to get rid of it as in the case of pus in an abscess.

ⁱ Auer (Proc. Soc. Exper. Biol. and Med., 1917-18, XV, 106) observed a localized edema in cats following the inhalation of dimethylsulphate. Generally one lobe or part of a lobe was involved. Auer expressed the belief that this localized fluid accumulation was due to the combination of a partial or complete stenosis of a bronchus or bronchiole along with an inspiratory dyspnea. "Under these conditions," he says, "each alveolus which is in connection with a stenosed bronchus or bronchiole will act like a miniature dry cup during inspiration because the pressure in these alveoli will decrease as the intrathoracic pressure decreases during each inspiration, for little or no air enters through the stenosed air passage. Therefore, during each inspiration which is slow, labored, and prolonged in the gassed cat, the capillaries of the alveolar walls are subjected to an aspirating action which facilitates or initiates the passage of a transudate into the alveolar spaces. The production of this transudate is probably also aided by a local damage of the alveolar epithelium which the war gas produces. Practically these observations may be of some value. In gassed soldiers all inspiratory dyspnea should be ameliorated as much as possible by tracheotomy and artificial respiration if necessary." While edema of the lungs produced by the commoner respiratory irritant gases is diffuse rather than localized, it is possible that the mechanism suggested by Auer, namely, bronchial constriction or obstruction, plus inspiratory dyspnea, may be a factor in bringing about the rapid and extensive fluid accumulation in the air sacs.

In other words, the edema is to be regarded as a purposeful reaction, which may, and if excessive undoubtedly does, lead to a certain degree of pulmonary embarrassment.

The importance of edema, as a cause of death, is discussed in the physiological section of this volume, but is considered here from the anatomical standpoint.

That the edema of the lungs is the immediate or direct cause of death from gassing by chlorine or phosgene seems to be taken for granted in most of the clinical reports of human cases.

Physiological studies likewise have tended to confirm the view that fluid in the pulmonary alveoli interferes with gaseous interchange and that when this interference with respiration passes a certain critical point, the patient dies of asphyxia, or, as popularly stated, drowns in his own fluid. A full dis-

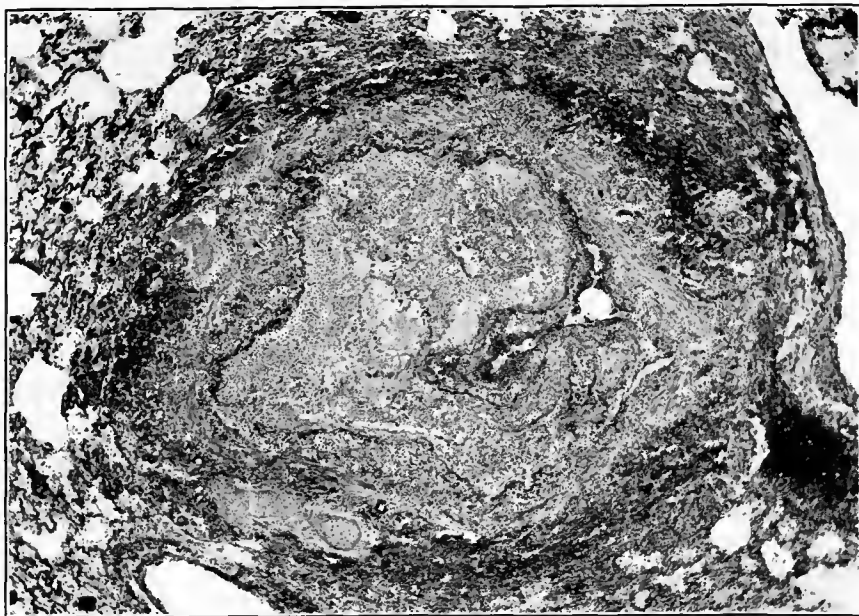


FIG. 86.—Complete necrosis of the mucosa of a large bronchus resulting from dichlorethylarsine gassing. There is a marked inflammatory reaction throughout the wall of the bronchus

cussion of the mechanism of death in gas poisoning is given elsewhere in this volume. (See p. 354.) There are presented here certain anatomic data which, it is believed, tend to show that undue emphasis has been placed on pulmonary edema as, *per se*, a cause of death. These observations, together with the results of some experiments upon what may be termed an artificial edema produced by filling the lungs of a normal dog with an isotonic solution have led not only to the questioning of the importance of pulmonary edema as a cause of death, but to the conclusion that edema of the lungs in general is merely an indication of some underlying disturbance, and is rarely, if ever, solely responsible for the death of the patient or animal.

The observations may be briefly summarized:

(1) Great variations are seen in the degree of pulmonary edema associated with death from acute gassing by any of the pulmonary irritant gases. With very high concentrations of gas or long exposures, death may occur quickly with little edema; on the other hand, sublethal exposures may give rise to marked edema with recovery. Animals recovering from gassing often show, when killed, a degree of edema greater than others which have succumbed. Furthermore, in certain species, such as rats and guinea pigs, the edema is inconspicuous, although the animals are quite as susceptible to gassing as other species in which edema is a marked feature.

(2) There is no relation between the degree of pulmonary edema and the concentration of the blood, which, as Underhill has shown, is a fair index of the seriousness of the gassed state.

(3) The lungs of a normal animal may be filled in great part with isotonic salt solution, thus producing an artificial edema, comparable in degree with that produced by gassing, without resulting in serious embarrassment of the respiration or circulation.

Several of the above propositions require some elaboration or discussion.

METHOD OF ESTIMATING DEGREE OF PULMONARY EDEMA

Marked differences in degree of edema may be readily judged by inspection and palpation, but for careful comparative study, a more accurate quantitative method, capable of expression in figures, is necessary. Such a method, based on the comparative weights of the lungs and empty heart, has been suggested and used by Barcroft in investigations carried on under the auspices of the British Medical Research Committee.²³ As used in the present investigations the method was as follows:

The lungs were weighed with the trachea attached, cut to uniform length, and clamped to prevent the escape of edema fluid. The heart was also trimmed uniformly and completely emptied. The normal ratio of the lung weight to the heart weight was obtained by taking an average of 16 normal animals. This normal ratio was found to be 1: 1.30, or simply 1.3. (Barcroft's higher figure, 1.5, is probably the result of a difference in the method of trimming of the organs.) In gassed dogs the lung weight was divided by the heart weight, and this quotient by the normal ratio, 1.30. The resulting figure was termed the "edema index." It represented the percentage increase in lung weight over the normal.

This method was objected to by Eyster,²⁴ who insisted that the dried weight method was much more reliable. There were two of these dried weight methods: One, used by some of the French investigators, in which a typical slice of the lung was weighed wet and then after drying, and the second, the method used by Eyster and his assistants, in which the entire lung was dried, the proportion between the wet and the dried specimen indicating the degree of edema. The first method was obviously open to large errors. The second method had the serious drawback of making it impossible to study the lung grossly or microscopically. The latter method was compared with the more simple lung-heart ratio in a series of six dogs, and it was found that the two methods gave results approximately the same (compare columns 9 and 13 in Table 59).

TABLE 59.—*Relation of the edema of lung and the concentration of blood in gassed animals.*

Dog No. and breed	Gas	Concentration per liter	Body weight	Weight of empty heart	Weight of wet lung	Weight of dry lung	Ratio of wet-dry lung	Ratio of weight of lung-heart	Red blood corpuscles before gas	Red blood corpuscles before death	Percentage increase of red blood corpuscles	Edema index
		<i>Mg.</i>	<i>Kg.</i>	<i>Gm.</i>	<i>Gm.</i>	<i>Gm.</i>						
1. Hound...	Phosgene...	82	14.0	155	715	-----	-----	4.60	5,148,000	7,936,000	54	3.53
2. Hound...	do.....	80	18.5	159	760	-----	-----	5.40	6,068,000	10,870,000	79	3.42
3. Mastiff...	do.....	75	26.0	170	915	-----	-----	5.40	8,400,000	10,808,000	28	4.15
4. Hound...	do.....	82	17.8	154	822	-----	-----	5.34	7,172,000	7,640,000	7	4.10
5. Collie...	do.....	99	17.8	177	570	-----	-----	3.22	6,192,000	11,290,000	82	2.48
6. Mongrel...	do.....	102	6.4	53	320	27.5	11.7	5.93	8,280,000	10,760,000	30	4.56
7. Mongrel...	do.....	112	8.6	92	400	37.0	10.8	4.35	9,385,000	9,824,000	5	3.34
8. Mongrel...	do.....	109	11.0	93	375	38.0	9.8	4.04	7,520,000	8,432,000	12	3.11
9. Mongrel...	do.....	109	6.8	69	219	24.5	8.9	3.16	9,848,000	9,055,000	-----	2.44
10. Setter...	Chloropicrin	949	13.6	132	631	61.0	10.3	4.77	8,040,000	12,120,000	51	3.68
11. Mongrel...	do.....	840	9.5	103	600	46.0	13.1	5.84	6,276,000	6,458,000	3	4.50
12. Bull.....	do.....	887	13.6	138	684	66.0	10.3	4.75	7,176,000	9,068,000	23	3.66

The dogs were killed 8 to 13 hours after exposure to phosgene or chloropicrin. Comparison of the figures in the last two columns (edema index and percentage increase in red blood cells) shows that no parallelism exists between the degree of pulmonary edema present and the blood concentration.

In using the lung-heart ratio method of estimating the amount of edema fluid present, it was found that the edema index in a series of dogs gassed under similar conditions varied within relatively wide limits. For example, among 50 dogs dying after exposure to phosgene, the edema index ranged from 1.73 to 4.60, and in another series, gassed with chloropicrin, the extremes were 1.65 and 4.22.

In order to throw further light on the question of the significance of the degree of edema, the following experiment was made: Eight dogs were gassed with phosgene (concentration 80 to 90 mgm. per liter for 30 minutes). Four of the dogs died in from 10 to 15 hours. The remaining four were killed by chloroform. It was found that the average edema index of the four dogs that died was practically the same as that of the four that were killed.¹ It was found also that many of the dogs which passed successfully through the critical forty-eight hour period and were then placed in the "recovered" group showed, if killed at this stage, a high edema index, often exceeding that of the dogs which had succumbed. It may be stated incidentally that these "recovered" dogs showed no symptoms other than occasional coughing and a slight sluggishness.

Still further evidence of the subsidiary part of edema as the cause of death after inhalation of irritating gases was found in the comparative effects of a gas such as phosgene on animals of different species.

A series of experiments was performed in which a number of different kinds of animals were exposed in the same chamber for thirty minutes to a concentration of 0.27 mgm. per liter of phosgene. The time of survival varied as indicated in Table 60

¹ Ricker, O. (Saniml. Klin. Vort. Inner. Med., Leipzig, 1919, Nos. 256-260, 727), in a study of the lung changes in cats gassed with phosgene, determined the degree of edema at varying intervals after gassing, using the weight method. Examination of his tabulated findings shows that one animal that was killed after 48 hours showed a greater edema than two others that died between 9 and 24 hours after gassing; a result that corresponds with our observations.

TABLE 60.—*Animals gassed with phosgene*

Species:	Time of survival
Monkey.....	3 hours 30 minutes.
Guinea pig.....	4 hours 30 minutes.
Rat.....	5 hours.
Rabbit.....	11 hours 30 minutes.
Mouse.....	Killed after 12 hours.
Dog.....	Killed after 12 hours.
Goat.....	Killed after 12 hours.

The lesions produced in these animals by inhalation of phosgene were essentially alike. In the monkey and goat, for example, which represented the two extremes of susceptibility after exposure to the same concentration, lesions of the lung varied in degree but not in character. The species variation, evidenced by the length of the survival after gassing, in animals which had been killed or had died, could be expressed in part by the rate of development of the pulmonary edema. On the other hand, with some animals (monkey, guinea pig), the first to succumb to a given concentration showed less pulmonary edema than those that survived longer (dog, goat). This is evidence that the edema was in itself not the cause of death but simply one manifestation of a more important underlying change.

While the pulmonary edema developed more rapidly the more susceptible the species (Table 60) the most susceptible showed at death less edema than the more resistant ones. This is an indication of the importance of the time interval in the production of the edema.

RELATION OF THE CONCENTRATION OF THE BLOOD AND EDEMA OF THE LUNG AFTER INHALATION OF GAS

Underhill ⁵ has found that dogs exposed to phosgene, chlorine, or chloropicrin showed after a few hours (the time varies with different gases and with individual animals) a well-marked increase in the concentration of the blood. Similar changes in the blood of gassed soldiers have been demonstrated repeatedly. The formed elements of the blood as well as the inorganic salts shared in the change. Inorganic salts, however, did not follow the same course as the erythrocytes. The result was a marked increase in blood viscosity. Underhill and his assistants used this blood change as an index of the condition of the gassed animals, and upon it have worked out a method of therapy, the essentials of which are bleeding and subsequent dilution of the residual blood with isotonic salt solution. In applying this method of treatment, which, it may be stated, has definitely reduced the mortality among experimentally gassed dogs, it has been assumed that the concentration of the blood was due to the escape of blood serum into the lungs, and that, therefore, the increased viscosity of the blood could be taken as a rough index of the degree of pulmonary edema.

In order to determine whether or not these two phenomena, blood concentration and pulmonary edema, were directly related, the following experiment was carried out. Twelve dogs were gassed, nine with phosgene and three with chloropicrin, the duration of exposure and concentration being such as would be fatal to a majority of dogs exposed. The dogs were killed with chloroform about 10 hours after the exposure to the gas; that is, as soon as the majority began to show serious symptoms. A red blood cell count was made before gassing and again just before the animal was chloroformed, since it has

been shown that this is a reliable method for estimating the degree of blood concentration. The degree of pulmonary edema found was determined by the method described above. The figures for the increase in blood concentration and the edema index are recorded in Table 59 with other data. The results are also graphically shown in Chart XXVIII. It is seen that under the condition of these experiments no parallelism existed between the amount of fluid present in the lung and the degree of concentration of the peripheral blood. It is noteworthy that in one case in which there was a well-marked edema of the lung, an actual reduction of blood concentration was found.^k This experiment

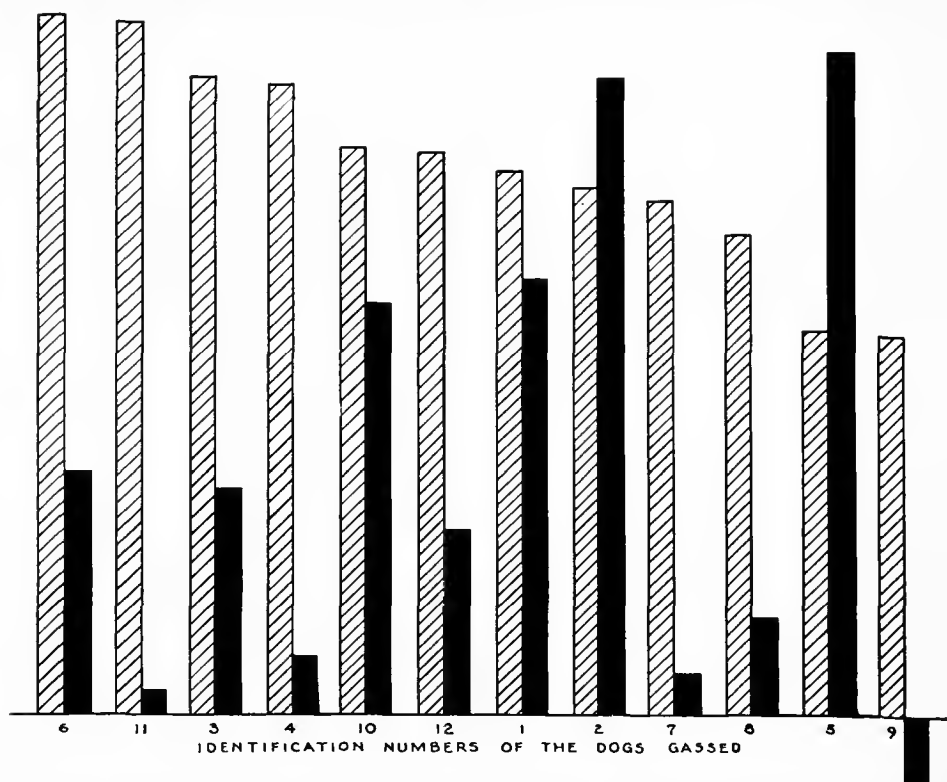


CHART XXVIII.—Comparison of the degree of pulmonary edema and concentration of the blood in gassed animals. Cross-hatched columns represent percentage of increase in lung weight and are arranged in order. Solid black columns represent percentage of increase in red blood corpuscles. This chart clearly shows that there is no relationship between the two

does not indicate that the loss of fluid from the blood may not have taken place by way of the lungs and the mouth, but, in our opinion, it does show conclusively that the change in the blood does not serve as an indicator of the amount of fluid present in the lung at any given moment. It suggests, further, that a therapy guided by the viscosity of the blood can not be assumed to have any influence on the pulmonary edema, and that the beneficial results obtained by such therapy are probably in no way referable to a change in the fluid content of the lung, which of itself is of secondary importance, as will be emphasized in the following paragraph.

^k There was dilution of the blood, as shown by Underhill, which preceded its concentration with phosgene poisoning. These changes of blood concentration may vary somewhat in duration, etc., and explain the charted findings above.

ARTIFICIAL EDEMA OF THE LUNGS. PULMONARY IRRIGATION

Winternitz and Smith¹² have shown that the lung is much less susceptible to the introduction of fluid than has been generally supposed. Repeated experiments have demonstrated that the lungs can be flooded through the bronchi with isotonic salt solution and that this process of irrigation can continue for at least two hours without causing any evident harmful changes in bodily well-being, or any subsequent serious microscopic lesions in the lung tissue. By means of the use of colored solutions it has been shown that the fluid introduced actually passes throughout the lung, bronchi, bronchioles and alveoli, and does not simply flow back through the trachea without entering the lung.

Examination of the lungs of dogs killed immediately after irrigation showed a marked "edema," comparable in respect to the amount of actual fluid in the lungs to that of the gassed animals. There was, however, little or no damage to the respiratory parenchyma, or the pulmonary circulation, and the fluid, as Winternitz and Smith have shown, was rapidly absorbed.

These data it is believed, support the conception of pulmonary edema in the gassed animal, stated in the earlier paragraphs of this discussion, namely, that it is a purposeful reaction and is not directly responsible for the animal's death.

BRONCHIAL DILATATION AND CONTRACTION

Several investigators, notably Schaefer, Hill, Gunn, Barbour and Williams, have studied the action of chlorine on the bronchi. Their methods have not been uniform, differing not only in the concentration of gas used, but also in the technique of exposure. These differences in method may account for some of the differences in their conclusions. Schaefer,²⁵ working first with the isolated animal lung and using a chlorine concentration of 1 to 10 or 1 to 20, observed no effect on the bronchial caliber, but in later experiments, with the lung in situ and respiration maintained with the Brodie pump, he noted a definite dilatation of the bronchi. Hill,⁶ on the other hand, using weaker concentrations of gas, saw no evidence of bronchial dilatation, but on the contrary thought that there might be some constriction of the bronchioles. In more thorough post-war studies on this problem, Gunn²⁶ reported as follows:

Generally, the results of experiments with chlorine have gone to show that inhalation of 1 in 5,000 up to 1 in 1,000 produces an increased rate of respiration with a transient bronchoconstriction. This bronchoconstriction is produced reflexly by the first contact of the irritant vapor with the bronchial mucous membrane. It lasts such a short time that the therapeutic measures to combat it would be unavailing. A subsequent sudden increase in the concentration of the gas may produce another transient reflex bronchoconstriction. Continued inhalation of the gas produces thereafter an apparent slight and gradual bronchoconstriction, but from histological observations, it appears probable that this is due rather to edema of the bronchial mucous membrane than to contraction of the bronchial muscle.

It is perhaps well to keep in mind that reflex effects arising from irritation of the upper air passages are excluded in these experiments. It is theoretically probable that irritation of the nasal and laryngeal mucous membranes will produce more immediate and possibly more intense reflex effects on the bronchi than will irritation of the trachea, for the sentinel posted in the latter region challenges the enemy gas too late.

A report of the physiology (war) committee of the Royal Society²⁷ on the pathology and treatment of pulmonary irritant gases contains the following paragraph on bronchial spasm:

In cases of accidental gassing by phosgene or chloropierin in factories, a frequent and distressing symptom is spasmodic asthma, which may recur even after brief inhalation of small

quantities of vapor. Well-marked constriction of the bronchioles has been observed as the result of inhalation of phosgene in animals (Golla). Exposure to chlorine has not been observed experimentally to produce this effect (Bayliss). It is not yet clear how far and for how long bronchial spasm may recur in men gassed in warfare. Laryngeal spasm may sometimes have been confused with bronchial spasm in man.

Barbour and Williams,²⁸ working in the Yale laboratories, exposed freshly excised bronchi of dogs and calves to the action of chlorine in Locke's solution, and noted that while low dilutions of the gas produced in some cases a transient relaxation of the bronchial musculature, concentrations of 200 milligrams to the liter, or more, regularly produced well-marked constriction which might or might not be preceded by a transient relaxation. These observers also noted similar reactions in the smooth muscle of the veins and arteries, but the constriction-producing concentration was found to be considerably lower in the case of the bronchi than in the vessels.

Both grossly and microscopically, there was seen, at autopsy in chlorine gassed dogs dying acutely, a dilatation of the bronchi of varying degree. But the dilatation was not pronounced and might have been due to mechanical obstruction of the bronchi by sloughs of necrotic membrane and exudate rather than to a direct action of the gas on the bronchial wall. In the delayed deaths, and more particularly in dogs recovering from severe gassing and killed some time afterwards, bronchial dilatation, or rather true bronchiectasis, constituted a very conspicuous feature of the lungs. In these cases, it seemed quite clear that the chronic infection with weakening of the bronchial wall, aided by obstruction resulting from the organizing bronchiolitis, was the chief etiologic factor.

Microscopically, changes suggesting a nodal constriction of the bronchioles were occasionally noted in animals dying acutely from both chlorine and phosgene, but upon careful study it was not determined that such pictures might not have been produced by twists or angles in the bronchial tree. Careful reconstructions would be necessary to settle this point.

CIRCULATORY DISTURBANCES

In discussing the subject of circulatory disturbances following gassing several questions, which are more or less closely interrelated, must be considered. Do the respiratory irritant gases directly damage the wall or contents of the pulmonary capillaries? If so, what is the nature of the injury or disturbance and what anatomical evidence is there that such changes affect the general pulmonary and systemic circulations?

Since the answer to the first question, to which the others are subsidiary, must be a qualified one, it is clear that much of the discussion of this problem must be to a certain extent speculative. There are, however, certain observations and deductions upon which most investigators are agreed.

For example, it is well established that exposure to very high concentrations of chlorine, phosgene, or chloropicrin may cause death in a few minutes, and that dilatation of the pulmonary vessels with stasis is the chief finding in such cases. Whether death under these conditions is due to a diffuse injury to the respiratory epithelium, or to vascular injury with dilatation, stasis, and consequent asphyxia, can not be stated, but the latter explanation appears the more plausible.

It is, however, in cases in which marked symptoms and death come on after some hours that the problem of circulatory disturbance is of most interest, and it is here that one finds disagreement as to the fundamental facts, particularly regarding the changes in the pulmonary vessels.

CAPILLARY THROMBOSIS

Klotz, in studying the action of chlorine on rabbits and mice, observed hyaline thrombi in the pulmonary capillaries and regarded them as the cause of serious obstruction of the blood flow through the lungs.¹

An important observation in the acute deaths, particularly in mice, was the finding of patches of diffuse coagulation of blood in the pulmonary capillaries. In these areas, we have observed within the capillaries and larger vessels the presence of a diffuse meshwork-like altered fibrin. Wide stretches of channels were found in which an irregular meshwork of threads stain diffusely blue with hæmatoxylin. In these thrombi relatively few red blood cells were found. Similar coagula with a varying number of erythrocytes were seen in the arterioles and venules. This process of thrombosis was not uniformly distributed through the lung.

Klotz¹ believes that embarrassment to the organism results from both failure of the right side of the heart and deficient oxygenation.

Dunn⁹ found in goats, killed by phosgene, capillary thrombi similar to those observed by Klotz in rabbits. In describing the changes in the initial period, that is, the first few hours after gassing, Dunn stated:

The cardinal feature is damage of capillary blood vessels in the zone where these are first exposed to the gas, with no greater protection than is afforded by the delicate pulmonary epithelium. The most striking evidence of injury of capillaries is the formation of thrombi in their lumina. When thrombosis is fully developed, it entails blockage of the affected vessels, so that the progressive exudation of fluid which continues long afterwards, must presumably occur from other vessels in which no microscopic change can be recognized.

In a discussion of the later changes, Dunn added:

The thrombosis of the capillaries undergoes very little extension after the end of the initial period and persists practically unchanged for 36 to 48 hours. It is always accompanied by much engorgement of the neighboring capillaries. * * * In animals living after 48 hours, there may be observed some absorption of the minute thrombi by phagocytes.

Perfusion of the lungs with salt solution failed to dislodge the thrombi, and the subsequent injection of carmine gelatin mass demonstrated that there was in places definite edema of the capillaries. The obstruction, however, was focal, rather than diffuse, large sections of the lung being well injected.

Rieker,²⁹ on the basis of extensive studies upon the action of phosgene on cats, emphasized the importance of dilatation of the vessels with resulting stasis, but did not attribute the disturbance to capillary thrombosis.

Similarly Winternitz and his coworkers have been unable to convince themselves that thrombosis occurs as a consequence of the injury by any of the pulmonary irritants, although they point out that the presence of a layer of fibrin along the alveolar walls in many cases, with threads crossing the septa (fig. 87; also see figs. 66 and 67) must constitute a definite barrier to the free flow of blood through the lung.¹

¹ Regarding the presence of thrombi in human lungs, following gassing, Pappenheimer says: "Our preparations show no clear evidence of thrombus formation, either due to agglutination of red blood cells, to ante-mortem fibrin deposition, or to the agglomeration of platelets in the pulmonary capillaries."

In view of the difficulty in recognizing a freshly formed capillary thrombus, which has little to distinguish it from a post-mortem clot, and lacks the character structure of mural thrombi in large vessels and heart, these conflicting observations are understandable.

As regards the significance of injection studies, it may be pointed out that, as Kline and Winternitz³⁰ have shown, great difficulty is found in perfusing and injecting the lungs in human lobar pneumonia, where outpouring of fibrin takes place even greater than that seen in gassed animals. The circulatory disturbance is probably much the same in the two conditions, in other words, equally obscure in etiology.

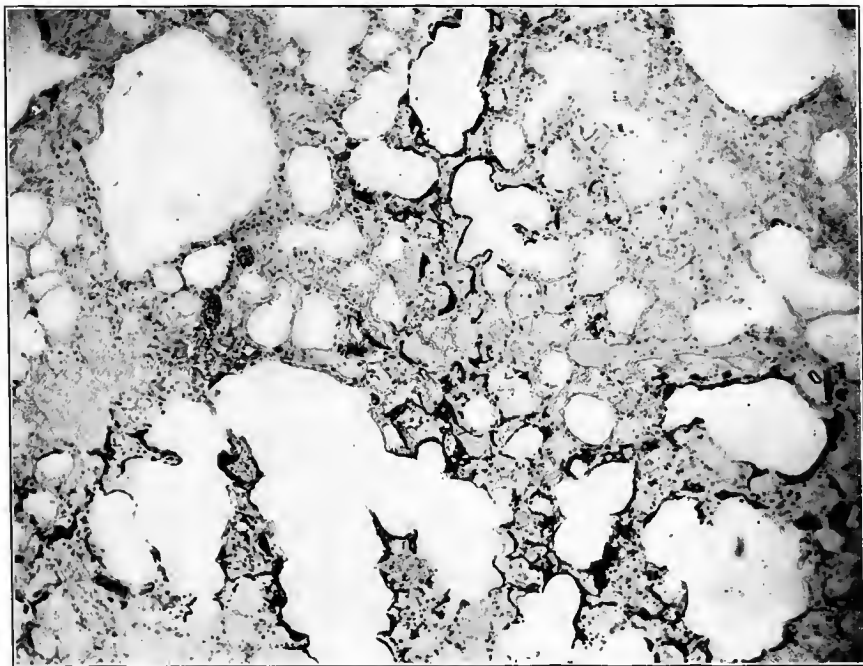


FIG. 87.—Thick layer of fibrin along the alveolar wall seven days after phosgene gassing

CARDIAC DILATATION

Much emphasis has been placed on the dilatation or at least the distention of the heart at autopsy, in acute deaths from gassing. In a report of the physiology (war) committee of the Royal Society, the following statement is made with reference to this finding:³¹

In fatal cases dying within 24 hours, the heart is usually found distended to a considerable degree with fully clotted blood. This is observed even when the post-mortem examination is made within two hours after death. When death occurs later, in about three days, dilatation is usually, though not invariably, observed.

In dogs the distention, of the right ventricle particularly, was often quite striking, and most observers have regarded it as an evidence of cardiac failure. Clinical observations, both in man and animals, have tended to confirm this impression. For example, according to Peters,³¹ among gassed soldiers examined within 24 hours after gassing, cardiac enlargement to the right was a

common finding; in some cases the heart border was as much as 1 inch to the right of the sternum. By X-ray photographs Bunting demonstrated a definite increase in cardiac outline in dogs gassed with phosgene. The discussion of the significance of these intravital observations does not lie within the scope of this chapter. But a recent study of the state of the heart at autopsy in cases where death was apparently not due to cardiac failure, suggests caution in attaching particular significance to post-mortem cardiac distention. Some of these observations may be briefly recorded. Six dogs, dying apparently from malnutrition in the course of feeding experiments, showed no general signs of circulatory disturbance; the heart in all cases, however, was more or less distended, as the measurements in Table 61 show:

TABLE 61.—*Dogs dying of malnutrition*

	Weight of heart		
	Full	Empty	Ratio
	<i>Grams</i>	<i>Grams</i>	
Dog 1.....	146	72	2.0
Dog 2.....	150	85	1.7
Dog 3.....	128	82	1.6
Dog 4.....	105	64	1.6
Dog 5.....	190	90	2.1
Dog 6.....	71	40	1.8

The heart measurements ^m in six dogs of similar size, which died within 24 hours after chloropicrin gassing, are shown in Table 62:

TABLE 62.—*Dogs dying of chloropicrin poisoning*

	Weight of heart		
	Full	Empty	Ratio
	<i>Grams</i>	<i>Grams</i>	
Dog 1.....	150	94	1.6
Dog 2.....	160	95	1.7
Dog 3.....	215	125	1.8
Dog 4.....	130	82	1.6
Dog 5.....	84.5	56	1.5
Dog 6.....	170	102	1.6

A comparison of the figures in the two series shows a slightly greater average cardiac capacity in the nongassed dogs. It might be added that a review of the findings in 20 additional chloropicrin dogs showed that the cases cited were representative. The average cardiac capacity of the entire series was, in fact, somewhat lower than that of the group from which figures are given.

In some observations on normal dogs killed by chloroform, the heart showed practically the same degree of distention as in the fatally gassed animals.

These findings do not, of course, invalidate clinical observations regarding the state of the heart during life, either in gassed animals or man, but they do suggest caution in the interpretation of autopsy findings with respect to cardiac dilatation.

^m Upon exposing the heart the great vessels were carefully clamped, then tied off with heavy cord and cut fairly close to the heart. Practically no blood was lost if care was exercised, and the difference in the weights of the full and empty organ showed very accurately the cardiac capacity.

HEMORRHAGES

Reference has already been made to hemorrhages in the pleura and endocardium of animals dying acutely from exposure to chlorine, phosgene, chloropicrin, and other gases of the respiratory irritant group.ⁿ In respect to size, location, and distribution these hemorrhages did not differ essentially from those seen in man in association with some of the severe infections or toxemias. In the lungs they were often overlooked at autopsy by the casual observer, owing to the extreme congestion and edema present, which obscured the picture. The posterior surface of the lung was the site of predilection, but gross extravasations were seen occasionally in the substance of the organ. Small foci in the lung, overlooked grossly, were frequently discovered upon microscopic examination.

The subendocardial hemorrhages were very conspicuous and not easily overlooked. They occurred most often in the left ventricle, were generally multiple, and distributed lengthwise along the crests of the muscular pillars and ridges. Now and then they were found about the bases of the valve cusps, mitral, tricuspid, and semilunar.

The hemorrhages in these acute deaths, though very striking in many cases, are of less significance than those seen in the chronic or recovered animals. It is the tendency to hemorrhage in this second type of animals that it is proposed to discuss here in some detail.

In the first series of autopsies on animals which had died five days to several months after gassing with phosgene and chlorine, hemorrhages in the lungs were recorded in approximately 35 per cent. The cause of death in a majority of these cases was respiratory infection of one type or another, generally bronchopneumonia, associated with an acute and chronic bronchitis.

In a second series of autopsies on "chronic dogs" that were killed 10 days to 5 months after gassing, for the purpose of studying the residual changes in the respiratory system, it was noticed that hemorrhages in the lungs were much more regularly encountered, the percentage being 90 as compared with 35 in the animals that died. Furthermore the hemorrhages were larger and more widely distributed. In most cases they were quite fresh, indicating that they had occurred just before death. These dogs had been killed with strychnine and all died in convulsions, which sometimes lasted several minutes.

In order to determine to what extent the convulsions were responsible for the hemorrhages, other methods of killing were resorted to. The dogs were divided into three groups. The first were killed with potassium cyanide (subcutaneous injection); the second with chloroform (forced inhalation); the third by a shot through the head from a small caliber pistol.

The dogs killed with chloroform were forced to breathe through an ordinary anesthetizing cone. Most of the animals struggled considerably. Hemorrhages in the lungs were found grossly in 60 per cent, and this figure was increased to 65 per cent by a microscopic study of the lungs.

The cyanide dogs died within a few minutes after the injections. Some showed only a slight rigor; in others there were definite convulsions, but never as marked or prolonged as in the dogs killed with strychnine. At autopsy the lungs showed hemorrhages in approximately 50 per cent.

ⁿ Punctiform hemorrhages in the brain in fatal cases of phosgene gassing in man have been described by Mott (*Brit. Med. Journ.*, 1917, i, 637) and by Rieker (*Samml. Klin. Fortr. Inner. Med.*, 1919, Nos. 256-260, p. 727). Similar lesions have not been recorded in gassed animals, possibly because the brains in most cases have not been carefully examined.

The dogs killed by shooting succumbed with less struggle than those killed with strychnine, chloroform, or cyanide. Hemorrhages were demonstrable in only 30 per cent, and in some of the positive cases the lesions were obviously not terminal.

From these observations, it may be concluded: (1) That hemorrhages occurred in a little less than 50 per cent of the "chronic" gassed dogs which died from respiratory infection or other cause; (2) that hemorrhages were present in a still higher percentage in dogs that were killed, the per cent varying with the method of killing, strychnine giving almost 100 per cent, shooting 30 per cent. In brief it appears that the lung of an animal that has been gassed is a favorable site for hemorrhage, and that hemorrhages into such a lung are easily induced by struggling or convulsions.

It should be added that 15 normal control animals were killed by the methods mentioned, and that while strychnia and chloroform produced hemorrhages in some cases, the lesions were never as extensive as in the gassed dogs.

The character of the pulmonary hemorrhages in these gassed dogs and the relation to the chronic inflammatory or reparative lesions so regularly found in the lungs of recovered animals are points which have interested us particularly. A brief description of the hemorrhages will suffice.

Grossly, the hemorrhages often resembled those seen in the acute stage; that is, they appeared as irregular subpleural extravasations of variable size and number situated generally on the posterior surface of the lung. But more often they occurred in the substance of the lung as nodules, generally irregularly spherical in outline. They varied in diameter from a millimeter to several centimeters. The larger ones were surrounded by a light zone of noncollapsed lung tissue, evidently the result of pressure of the hemorrhage on a bronchus. The relation of some of the smaller hemorrhages to bronchi was often quite clear, particularly in dogs killed in the subacute period, 5 to 10 days after gassing. The hemorrhagic foci in these cases were seen to coincide with the fine nodules of organizing bronchiolitis. (See Pl. XIII.)

Now and then an extravasation of blood was seen forming a sort of halo about a fair-sized artery in the lung. (Fig. 88.) This is the so-called "ring hemorrhage" which was obviously the result of the rupture of one of the vasa vasorum, with the escape of blood into the perivascular sheath. Similar hemorrhages have been described by Mott⁷ in the human brain, following fatal phosgene gassing, and by Ricker²⁹ in cats experimentally gassed.

The question naturally arises as to whether there is any relationship between these hemorrhages and the chronic infection and reparative changes which characterize the gassed lung. In answer it can be stated, on the basis of microscopic examination of a large number of lungs, that in practically every case in which hemorrhages were found, residual focal lesions, generally of the nature of an organized bronchiolitis, were demonstrable. Furthermore, in many cases, especially in dogs killed in the subacute period (5 to 10 days after gassing), the hemorrhages were seen to originate directly in these lesions. (See Pl. XIII.)

In addition to fresh hemorrhages one saw not infrequently patches of disintegrating blood cells and scarred areas containing blood pigment. The presence of these would suggest that hemorrhages were not only the effect of

a scarred damaged lung, but might also have been the cause. The delicate vessels of the scar were prone to rupture. The resulting hematoma became organized with the formation of more scar tissue. In other words, it seems possible that in these chronic lesions of the lungs and in hemorrhages there may have been a vicious circle, with sudden increase in blood pressure (induced by excessive physical effort, struggling convulsions, or other cause), as the force which kept the process going.

The conclusions to be drawn from the foregoing observations upon hemorrhages in the lungs of chronic gassed animals are: (1) The chronic inflammatory and reparative changes in these lungs created a condition favorable to hemorrhage; (2) hemorrhages were induced in such lungs by sudden increase in blood

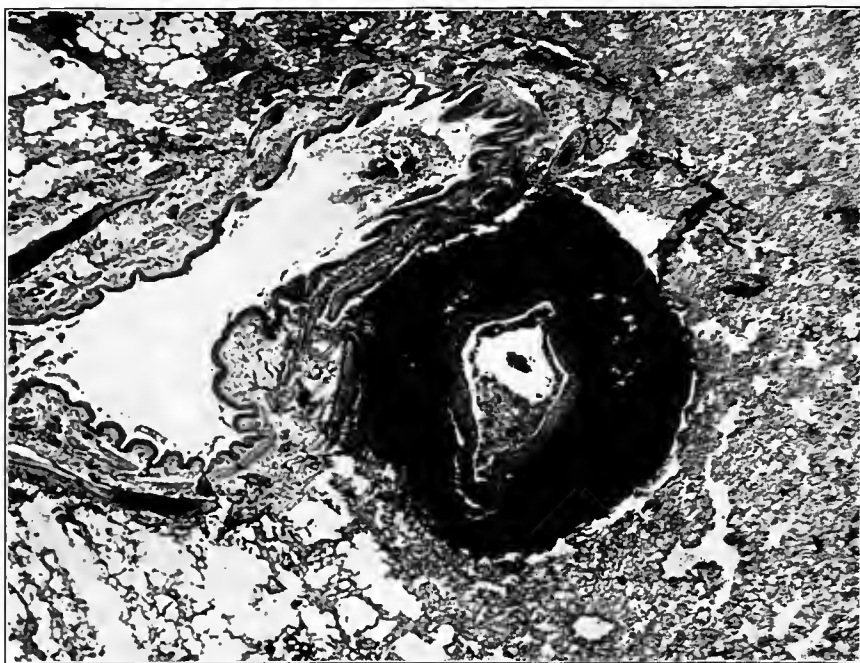


FIG. 88.—Hemorrhage into a perivascular sheath of a pulmonary vessel in a dog dying 10 days after phosgene gassing

pressure; (3) hemorrhages might lead to further scarring of the lung, which again favored bleeding, thus constituting a vicious circle.

RESPIRATORY INFECTION

A marked tendency to respiratory infection, after exposure to irritant gases, has been observed in both man and animals. The most outspoken examples of such infection were seen in cases where the gas injury was severe, but not sufficient to cause death within 24 hours. A widespread necrotizing bronchopneumonia was the usual result in these cases.

Several questions present themselves in respect to the origin of the infection and its manner of spread.

Even within a few hours after gassing, particularly in the case of chlorine, a definite inflammatory reaction was seen in the lungs. Apart from the edema, the inflammatory nature of which may be considered debatable, one found in



FIG. 89.—Necrosis of bronchial epithelium with acute inflammatory reaction 24 hours after chlorine gassing

the alveoli, small quantities of fibrin, few scattered polynuclear leucocytes, and occasional large mononuclear (epithelial) cells, and in the capillaries a definite polynuclear cell increase. This mild reaction was fairly diffuse and may be interpreted as a reaction to the chemical injury.

Six to twelve hours after gassing (often longer) another type of reaction, clearly focal in origin, was frequently seen. The chief element in the exudate was the polynuclear leucocyte, and the location was most often in and about the bronchiole. (See figs. 54 and 68.) In the case of chlorine a similar reaction was found also in the walls of the large bronchi and trachea. (See fig. 61.) The question has been raised as to whether this early inflammatory process was a response to the chemical injury or to a complicating infection. In view of the difficulty in demonstrating bacteria in sections at this stage, it has been argued that the reaction was a direct response to the gas injury. It seems to us, however, that for several reasons, this interpretation of the reaction can not be maintained: 1. The difficulty of demonstrating bacteria in sections is well

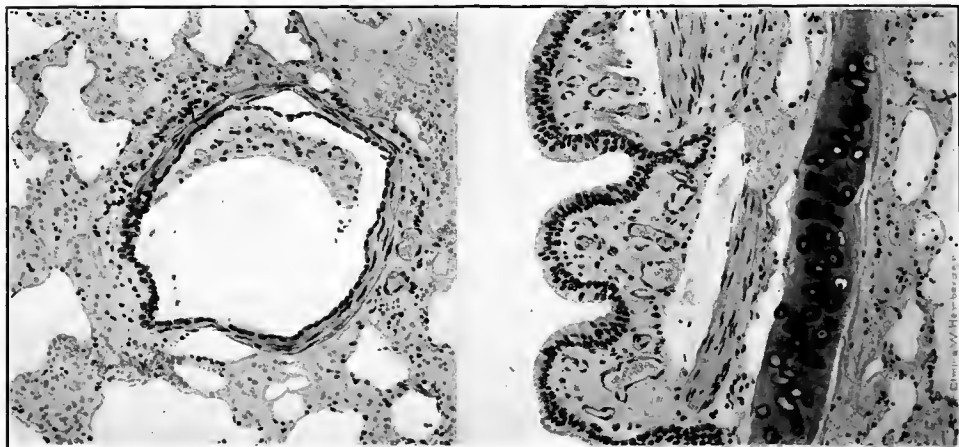


FIG. 90.—Wall of small bronchus showing mucosa entirely destroyed by phosgene and a large bronchus of same animal with uninjured mucosa

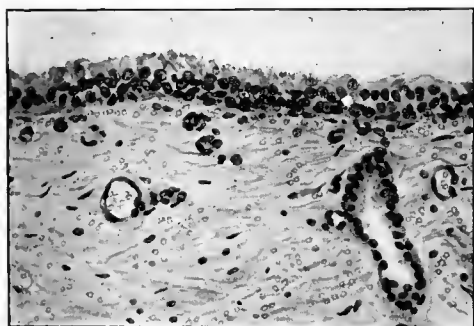
recognized, and negative findings are therefore not conclusive. 2. Cultures show that bacteria are present in the lungs of a high percentage of gassed animals, and in practically all cases in which a frank pneumonic reaction has developed. 3. The character of the exudate, which is predominantly polynuclear, the focal distribution of the lesions, and the localization about the atria suggest a reaction to a bacterial rather than to a chemical injury.

Furthermore, it has been pointed out (Smith) that the similarity of the organisms found in the lungs of gassed animals with those present in the mouths of normal dogs indicates that the organisms make their way from the mouth to the lung shortly after gassing. In support of this idea the following observations on two series of chlorine gassed dogs are presented:³²

In the first series, the lungs from 25 animals were cultured. These include dogs that lived 12 hours to 48 days after exposure. In 6 cases, cultures were negative. In 1, a pure culture of a small Gram-negative hemoglobinophilic bacillus was recovered. In 12, pure cultures of pneumococci resulted, and 6 cases, both the pneumococcus and the small Gram-negative bacillus were

obtained. In five of the animals post-mortem blood cultures were also made. Two of the animals had died 24 hours after gassing, one after 3 days, one after 6, and one after 36 days. In all of these, pure cultures of a Gram-positive diplococcus, similar to that found in the lungs, were recovered.

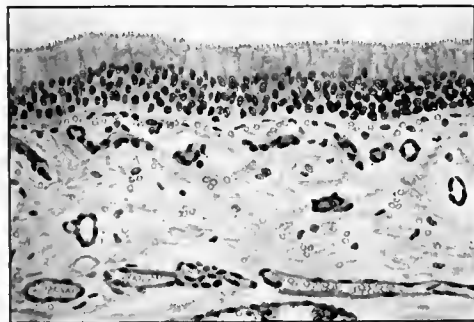
A more detailed study was subsequently carried out on a series of 21 dogs. In these the normal flora of the mouth was first determined. The cultures were made on two successive days, prior to gassing. In addition to such common organisms as streptococci, staphylococci, and *B. subtilis*, there were found in the mouth of each of the dogs, a Gram-positive diplococcus that agglutinated with pneumococcus group 2 serum, at a dilution of 1 to 2, and a small Gram-negative hemoglobinophilic bacillus very similar to the influenza bacillus. In



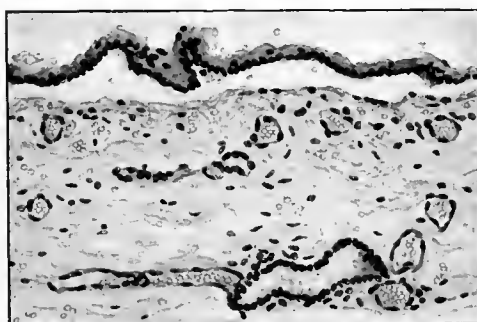
A



B



C



D

FIG. 91.—A comparison of the injury to the tracheal mucosa by chloropierin, phosgene, and chlorine. A, Chloropierin, with damaged but intact epithelium; B, chloropierin with sloughing of superficial epithelial layer; C, phosgene, with undamaged mucosa; D, chlorine, with killed and exfoliated mucosa

14 cases both of these latter organisms were found, while in 6 the pneumococcus alone, and in the Gram-negative bacillus alone was obtained.

The lung cultures taken post-mortem were negative in 4 cases where death resulted shortly after exposure. In 9 cases the pneumococcus alone was obtained. In 4 the pneumococcus and the Gram-negative bacillus were recovered, and in 4 others the Gram-negative bacillus alone was recovered.

Blood cultures (post-mortem) were positive in 5 of the 21 animals. The organism recovered in each case was the pneumococcus.

The conclusion from this study is that organisms which normally inhabit the mouth of the dog find their way into the lungs shortly after gassing and remain there for a long time in animals that survive the acute stage.

RESIDUAL PULMONARY LESIONS

Animals recovering from moderately severe exposures to any of the pulmonary irritant gases showed, even up to five months after gassing, definite residual lesions in the lungs of greater or lesser degree.* These changes have been fully described and illustrated in the reports on the pathology of chlorine and phosgene gassing. They probably occurred quite as regularly after exposure to other gases, which have not been as fully studied. The question to be considered here is that of the significance of the lesions, and particularly their bearing on certain clinical phenomena, effort-syndrome, tendency to chronic respiratory infection, etc., observed in human gassed cases and regarded as late effects of the gas injury.

Subjective symptoms in dogs obviously did not admit of investigation, but the general appearance of the animals, weakness, loss of weight, tendency to cough on exertion, suggested a condition in the recovered gassed animal similar to that in man. No reports have been found of systematic clinical or physiological studies of animals such as have been made by Lewis, Barcroft, Pearce, and others in man.

Regarding the nature of the anatomical findings in these dogs, little need be added to what has gone before. They varied in individual animals, and to some extent with different gases. In the more pronounced cases, which ended fatally, there was a suppurative bronchitis and bronchiectasis, with occasionally a chronic infection of the lung tissue itself, that is, an organizing or interstitial pneumonia. In the majority of animals, however, the lesions were healing or healed, and were limited to certain of the smaller air passages and the lung tissue supplied by these. The bronchioles were partially or completely obliterated; the tributary lung tissue was atelectatic or emphysematous.

The frequency and general character of the changes found in recovered dogs are very well shown in Table 50 (p. 429) for chlorine, and Table 54 (p. 450) for phosgene. It is seen that of the chlorine dogs which died or were killed from 15 to 193 days after gassing, 51 per cent showed bronchitis of one type or another, and 24 per cent pneumonia. Organization was a feature of both the pneumonic and bronchial lesions. Of the phosgene dogs, 60 died and 103 were killed two weeks to four months after gassing. Bronchitis was demonstrated in 68 per cent, pneumonia in approximately 10 per cent. These figures are based on gross findings confirmed by one or more microscopic sections. It is very certain that a more thorough microscopic examination in all cases would have increased these percentages considerably. Indeed, after reviewing a large amount of material it is our impression that a severe exposure to practically any of the respiratory irritant gases—phosgene, chlorine, and chloropicrin particularly—makes for a permanent and usually demonstrable damage to some part of the respiratory tract. The effects on the respiratory tract of repeated (sublethal) exposures to irritating gases has not been systematically investigated. But it has been the impression, from a routine examination of the organs of a number of dogs killed after two or three exposures to chlorine or phosgene (intervals of ten days or more), that the residual or chronic changes

* The organic arsenicals would appear to be exceptions to this general statement in that according to Finney's studies none of the recovered dogs showed any residual lesions. In view of the fact, however, that such lesions were found after mustard gassing, the effects of which are so similar to those of the arsenicals studied, one is inclined to think that a more thorough investigation of Finney's cases would have shown chronic pulmonary changes.

in the lungs were much more marked than in dogs recovering from a single gassing. There is, of course, nothing remarkable in this observation; although it is of interest here that Underhill⁵ did not observe, in the case of phosgene at least, that animals previously gassed were more susceptible to a second gassing, as judged by symptoms and mortality figures.

If lesions analogous to those described in dogs follow gassing in human beings (and there is no reason to suppose that they do not) there would appear to be a clear anatomic basis for the clinical phenomena observed. In this connection the following quotation regarding changes characteristic of the period of convalescence, from a report compiled by the physiology committee of the Royal Society,²⁸ is of interest.

Clinical observations (T. Lewis, Riddell, Price, Jones, and Hunt) indicate that, temporarily, as large a proportion as 36 per cent of their gassed subjects may exhibit the so-called "effort-syndrome." There seems no sufficient reason to assume in such subjects a specific change in the tissues of the lungs which might be held accountable for such a symptom as breathlessness; in some cases, though not in all, there are grounds for believing that in the earlier asphyxial stage the heart may become permanently strained. There is no evidence of a permanent dilatation of the organ, though this point has been carefully investigated. In the various cases admitted into the special hospitals for the heart, gassing is regarded as a relatively unimportant cause, and where it occurs in the histories it is stated that in as many as 30 per cent the men were at the time of gassing probably affected with the condition which exhibits the "effort-syndrome" (T. Lewis). The condition, as far as gassing is concerned, must be regarded as a feature of convalescence, and not as a persistent stage.

The question of cardiac dilatation after gassing has been discussed in another paragraph; here the doubtful value of post-mortem evidence is pointed out. A review of the figures upon the weights of the unopened and empty hearts in a large series of gassed dogs, shows that, in general, the capacity of the heart is greater in delayed than in acute deaths, but, as previously emphasized, the figures are practically the same as for animals dying from other conditions, so that it seems unjustifiable to draw any conclusions from these data.

The pulmonary lesions in dogs were clearly regressive, just as the tendency to recovery indicates that they are in man. Ten days after severe but not fatal gassing with phosgene or chloropicrin, the dog's lung was studded with readily palpable and visible tubercle-like nodules of organizing bronchiolitis, whereas a month after gassing these foci were practically microscopic, unless, as happened in a certain percentage of cases, a complicating infection had persisted.

Definite evidence of the persistence of pathogenic microorganisms in the lungs of these recovered animals was obtained by making lung cultures in 31 cases. The dogs had recovered from a moderately severe exposure to phosgene and were killed at varying intervals after gassing. Cultures from the small bronchi and lung tissue itself were taken promptly after death, using broth and blood agar. The findings were as follows:

Staphylococcus aureus.....	5
Streptococcus hemolyticus.....	5
Streptococcus nonhemolyticus.....	2
B. subtilis.....	4
Miscellaneous organisms.....	5
No growth.....	10

It is seen that the lungs were sterile in less than a third of the cases, while pathogenic organisms were present in approximately 50 per cent.

From these observations it may be inferred, therefore, that the lung of the gassed animal or human being is the seat of chronic infection which may at any time become active and dangerous.^p It is clear also that the disability manifested by a certain number of gassed individuals may be due partly to mechanical interference with proper respiratory exchange from bronchiolar obliteration, emphysema, etc., and partly to the noxious effects of a persistent respiratory infection.

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CHAPTER XV

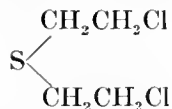
PATHOLOGIC ACTION OF MUSTARD GAS (DICHLORETHYLSULPHIDE)^a

HISTORICAL NOTE

The discovery of dichlorethylsulphide and the recognition of its toxic action have been usually ascribed to Victor Meyer in 1886.¹ A more intensive searching of chemical literature than was possible during war time carries knowledge of this subject back to 1860 and to the researches of an English chemist, F. Guthrie,² who contributed a study on some of the derivatives of the olefines, including an investigation of the action of sulphur chloride on ethylene, and studied the product of this action, which he designated *Aethylendichlorosulfid*, and to which he gave the formula $C_4H_4S_2Cl_2$, described this product as having a pungent, not unpleasant odor similar to mustard oil, with an astringent taste like that of horse-radish. As to its pathologic action, he noted that the small amount of vapor arising from it attacked the more tender parts of the skin, as, for example, between the fingers and around the eyes, and destroyed the epidermis. When applied in liquid form to the skin there developed a blister.

In the same year, A. Niemann³ studied the action of the brown sulphur chloride upon ethylene, and obtained an impure product to which he gave the formula $C_4H_4ClS_2$, as most closely corresponding to the results of his analysis. He described this as possessing an odor similar to horse-radish oil, although less penetrating. The most characteristic property of the substance, however, was that regarded by him as most dangerous, in that the slightest trace of the liquid coming into contact with the skin caused at first no pain; but after several hours there developed at the point of contact a reddening, followed on the next day by the formation of a blister which very slowly suppurated, and which was extremely slow in healing, with the production of a marked scar. He noted the occurrence of these toxic effects in the same manner in different individuals, and warned against the danger of working with this product.

No further work upon the action of sulphur chloride upon ethylene appears to have been carried out until Victor Meyer¹ succeeded, in 1886, in producing a pure dichlorethylsulphide, to which he gave the name thiodyglykolchloride, with the formula:



In addition to a description of the chemical properties of this substance, Meyer noted also observations upon its toxic action. He considered it as most striking that this substance, apparently harmless, so slightly volatile, and almost insoluble in water, of very slight odor and neutral in reaction, and from its chemi-

^a The material forming the main body of this chapter is taken from the investigations of Warthin and Weller, published as "The Medical Aspects of Mustard Gas Poisoning," C. V. Mosby Co., St. Louis, 1919. These experimental studies first appeared in the *Journal of Laboratory and Clinical Medicine* during 1918-1919; the first study, that on mustard-gas lesions of the skin, was published independently. After its publication the pathological laboratory of the University of Michigan became allied with the medical advisory board of the Chemical Warfare Service, and the first reports of the remaining investigations were given that board and published in abstract in its bulletins, later appearing in the Journal mentioned. The literature of the subject was consulted, and differences of opinion and new observations were given full consideration.

cal constitution giving no expectation of aggressive properties, should exert such a specific toxic effect as it produced upon one of the workers in his laboratory in the form of severe skin lesions and a transitory inflammation of the eyes. As Meyer himself was not affected by his work with it, he was at first inclined to believe that its toxic effects were due to some individual idiosyncrasy. At his request animal experiments were carried out with the following results: Two medium-sized rabbits were confined three to four hours in a closed chamber, ventilated by a moderately strong current of air entering through a glass tube containing strips of filter paper saturated with thiodiglykolchloride (dichlorethylsulphide). The animals became restless, and rubbed their noses and mouths frequently with their paws. The nose, mouth, and conjunctiva became very much reddened and the eyes very moist. Perspiration appeared to be increased. On the following day the eyes were severely inflamed, the lids glued together by purulent secretion. Marked snuffles developed, the lobes of the ears were much swollen and the external auditory passage showed a purulent inflammation. On the evening of the third day the animals died, and the lungs of both showed a severe diffuse pneumonia. A larger-sized rabbit that had inhaled the vapor of the substance through a tracheal fistula for a few hours, with the surface of its body protected from contact with this vapor, died on the evening of the same day from a diffuse pneumonia, before other symptoms had had time to appear. In rabbits whose ear-tips had been painted upon the unbroken skin with a small amount of the chloride by means of a fine pencil, no direct local effects were seen, but the entire ear became greatly swollen, and in one case a profuse purulent inflammation developed. Because of the small amount used and its external application, any entrance of the material into the external canal was excluded. In one case in which the hairs had been removed from the tip of the ear the local touching with the chloride produced a suppuration at the point of application, with an associated diffuse swelling of the whole ear and inflammation of the eyes. After subcutaneous injection of about two drops of the chloride into the back of a rabbit there developed an inflammation of both eyes and severe snuffles, with death on the third day from pneumonia. No effects were noted at the point of application. Because of the fact that the vapor of the chloride affected those engaged in this experimental work, it was discontinued. Meyer concluded that the toxic action reached its height only after its entrance into the blood stream.

During the next year Meyer⁴ made a second contribution on the physiologic action of dichlorethylsulphide. Through further investigations he had found that the slightest trace of this substance produced on human skin severe and prolonged inflammations. Rabbits, after a short exposure to its vapor, died regularly with pneumonia, and the local application of a trace of the substance to the ear produced severe inflammation of the ear and eyes, with marked swelling of the former. He noted also that animals surviving such a local application showed a persistent profuse suppuration, leading, after several weeks, to a complete necrosis and loss of the ear. Physiologic tests were made also with the monochlorethylsulphide, which was found to possess similar, although less intense, toxic properties. Chlorine-free ethylsulphide was also tested as to its physiologic action and found to be nontoxic. Meyer decided, therefore, that the toxicity of the mono- and dichlorethylsulphides depends entirely upon their chlorine content.

The remarkable toxic properties of this apparently nonaggressive substance seem strangely to have escaped the notice or interest of pharmacologists. It is apparently not mentioned in the literature again until 1891, when Th. Leber,⁵ on the ground of the two experimental studies of its action on the eye which he had made for Meyer in 1886 and 1887, concluded that dichlorethylsulphide belongs to the pus-producing class of inflammatory irritants.

It again falls back into obscurity for a period of over 20 years. No mention of the physiologic action of this substance is found again until 1912, when H. T. Clarke,⁶ corroborating Meyer's findings concerning the poisonous action of dichlorethylsulphide, made the following statement:

That its action is toxic, and not merely irritative, as is the case with acids, is shown by the absence of pungency in the odor and by the fact that it takes effect only after some hours have elapsed. It can, nevertheless, be handled with perfect safety, provided that care is taken not to inhale its vapor, or to allow it to come into contact with the skin.

After another period of neglect, as far as the literature of the subject is concerned, dichlorethylsulphide was forced upon the attention of a war-distraught world in a most sensational manner through its successful employment on a large scale by the German Army as a war gas, at Ypres, July 12 and 13, 1917.⁷ From that time to the end of the war it proved to be their most effective war weapon, although the protective measures devised against it by the Allies led to a great reduction in the number of casualties caused by it. Within eight days after the first bombardment with this substance the peculiar physiologic effects produced by it led Lieut. Col. Harrison and Professor Baker to conclude that the active constituent of the gas shell must be dichlorethylsulphide, as described by Victor Meyer, and this supposition was confirmed a few days later by the chemical analysis of the shell liquid.

The recognition of the new poison gas as dichlorethylsulphide naturally developed an intense interest among the scientific men connected with the Allied armies, as well as in various scientific institutions and laboratories not directly connected with the armies, but engaged on problems of research relating to the war. In the pathological laboratory of the University of Michigan, at Ann Arbor, there had been begun an intensive study of poison gases that might be employed in warfare, as the especial war-problem of this laboratory.^b Studies on chlorine were being prosecuted when news of the new gas was received. The laboratory was soon placed in possession of a quantity of pure dichlorethylsulphide through the kindness and skill of Dr. Moses Gomberg, of the chemical laboratory of the university.

Pure beta-beta-dichlorethylsulphide as prepared by Gomberg was a clear, colorless, heavy, oily fluid, having a very faint cress or mustardlike odor, more like that of a freshly bruised plant than that of prepared mustard. The boiling point was 217° C. Samples of this preparation were unchanged when nearly five years old. Later, other samples of mustard gas were received from various sources, and these were all more or less impure, having a slight or marked yellowish or brownish color and a more decided odor. With age these impure samples became more brownish and more odorous. The pure substance caused no staining of tissues with which it came in contact; the impure substance sometimes stained tissues a bright yellow. These impure samples varied between 60 to 85 per cent of dichlorethylsulphide content and were, therefore, comparable to the percentages actually employed by the Germans in their yellow cross and green cross shell.

^b These investigations were made by Doctor Warthin and members of his staff, Dr. C. V. Weller and Dr. George R. Hermann.

The studies on which this chapter is based took up, in turn, the pathologic action of mustard gas on the skin, the eye, the respiratory and gastrointestinal tracts, and finally its general pathologic action. They were concerned with the gross and microscopic lesions produced both in man and animals by the direct application of the liquid dichlorethylsulphide or by exposure to its vapor. The human material was obtained through auto-applications, amputation material with consent of the patient, and accidental lesions in laboratory workers or in men engaged in the manufacture of dichlorethylsulphide. By means of auto-applications complete series of lesions in all stages from inception to healing were studied. In factory workers all types of mustard-gas burns were observed, from the mildest forms to those of the greatest severity ending fatally. Lesions were produced in all possible ways by the direct application of pure mustard gas and its solutions of all possible strengths, and by exposure to varying concentrations of its vapors. To standardize the results a method of applying a known quantity of liquid mustard gas was devised by the use of a standard capillary pipette which would deliver uniform droplets estimated at about 0.0004 c. c. For the vapor exposures an especial gassing chamber was constructed for animal work, whereby known concentrations of the gas could be employed. (See fig. 190, p. 596.)

Mustard gas is essentially a local poison, exerting its action directly upon those tissues with which it comes into contact. The very mildest concentrations of its vapor usually affect the eyes first, then the skin and the respiratory tract. Stronger concentrations of its vapor usually affect the eyes first, then the skin and the respiratory tract. Stronger concentrations may act first upon the skin, particularly upon delicate or sweaty cutaneous areas as the genitalia and flexor surfaces; or skin, eyes, and respiratory tract may be affected at the same time. The cutaneous lesions, on the whole, are the most common and striking; the respiratory lesions, however, are the ones most likely to produce serious results, when they are severe. The toxic action of mustard gas on the skin, eye, respiratory and gastrointestinal tracts, and its general pathology are given in order. When a series of animals was used for individual experiments one typical protocol alone is given to illustrate it, but the final conclusions are based upon the total number of controlling investigations carried out.

CUTANEOUS LESIONS PRODUCED BY MUSTARD GAS APPLIED IN LIQUID FORM

ACTION ON HUMAN SKIN

Dichlorethylsulphide was applied by means of a capillary pipette in uniform droplets estimated to be about 0.0004 c. c. When applied to the skin this drop at once spread out over an area 3 to 4 mm. in diameter and was completely volatilized, or at least disappeared, in one to two minutes, according to atmospheric conditions.

Following is a protocol of the most important stages in the development of the skin lesion produced in this manner. It was found that the rate of production of the lesion and the intensity of the reaction varied over a considerable range in different individuals; notable in a Charcot-joint leg and in a case of malignant disease the development of the vesicle was delayed.

AUTO-APPLICATION TO SKIN OF NORMAL INDIVIDUAL
PROTOCOL

March 12, 1918, 2.30 p. m. Standard droplet applied to flexor surface of left forearm. In one minute the liquid completely disappeared, giving off a strong odor. There were no subjective symptoms. In about 10 minutes there appeared a delicate silvery gray sheen over the surface of the area of application. This was soon followed by a faint flush, which gradually deepened and spread until it was about 7 mm. across. Photograph (fig. 92) was taken one hour after application. At this stage the erythema was influenced by changes of temperature, etc., alternately paling and reddening. Whenever the area became somewhat paler the superficial silvery luster was visible. During the second and third hour a well-marked edema appeared and the erythematous zone became wider and more deeply colored.

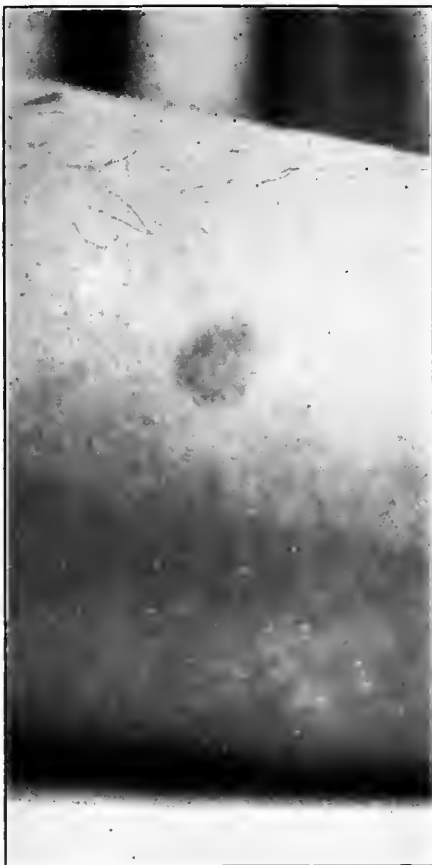


FIG. 92.—Mustard-gas lesion at one hour

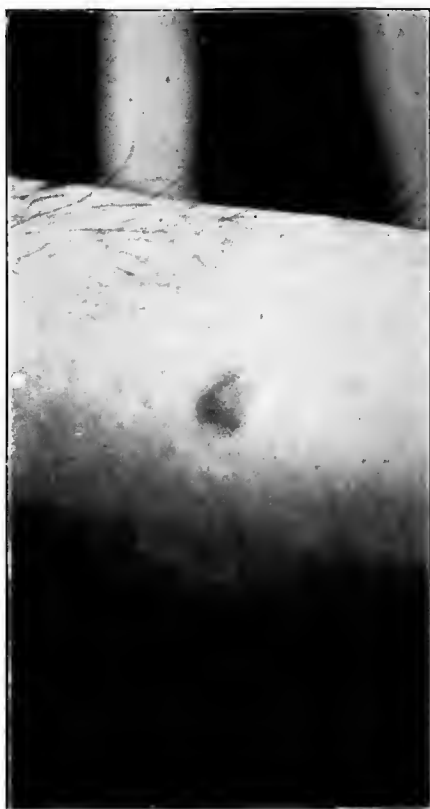


FIG. 93.—Mustard-gas lesion at three hours

Same day, 5.30 p. m. At this time the lesion measured 15 mm. in diameter. It was slightly elevated and had a marginal zone somewhat deeper red than the central portion. Outside of the red zone there was a very faint, barely perceptible zone showing less color than the remainder of the skin. (Fig. 93, photograph three hours after application.) In the next several hours there was no change.

March 13, 1918, 6.30 a. m. Sixteen hours after the application a vesicle began to form. At 8.30 a. m., 18 hours after the application, this was at its height. (Fig. 94.) At this time the lesion measured 25 mm. in diameter. It presented an erythematous base, slightly elevated, and fading gradually into the surrounding skin. Upon the summit of this erythematous base there rose a tense vesicle 6 by 9 mm. in area and 3 mm. high. This was

filled with a clear pale-yellow fluid. Up to this time there had been no subjective symptoms, but with the formation of the vesicle there was slight smarting, increased by pressure.

Same day, 12.30 p. m.—22 hours after application. (Fig. 95.) At this time the vesicle covered no greater area but was 4 mm. high and still very tense. Its fluid content had become slightly cloudy or opalescent. With a hand lens the base of vesicle could be seen through the fluid content and appeared yellowish-white, opaque, and necrotic. Around the border of the inflamed base of the vesicle there was a definite secondary areola.

March 14, 1918, 12.30 p. m.—46 hours after application. (Fig. 96.) By this time there was nearly complete absorption of the fluid from the vesicle. The epidermal covering of the vesicle was thrown into fine wrinkles and folds and had taken on a yellowish-brown

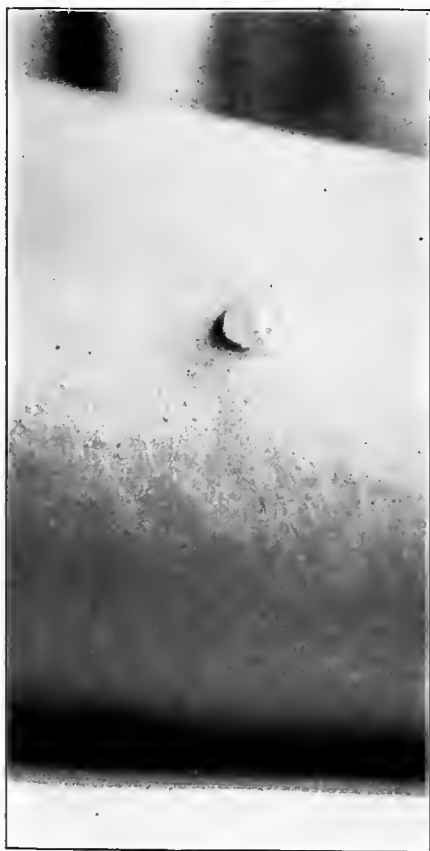


FIG. 94.—Mustard-gas lesion at 18 hours



FIG. 95.—Mustard-gas lesion at 22 hours

tint. The zone immediately around the base of the vesicle was pale pinkish-white and about 1 mm. in width. Outside of this the flushed areola persisted. The total width of the lesion was but 17 mm.

March 15, 1918, 2.30 p. m.—72 hours after application. (Fig. 97.) The central portion of the lesion measured 8 by 4 mm. and was of a bright yellowish-brown color. Around this was a white zone 1 to 2 mm. in width. Outside of this was a zone of erythema most marked about the base of the collapsed vesicle and fading peripherally. The total width of the lesion was 18 mm.

During the night of March 15 to March 16 the delicate wrinkled epidermis was rubbed off, leaving an excavated area with a grayish yellow-white moist base. The excavated area measured 6 by 4 mm. The border was somewhat irregular and slightly overhanging. The white zone, about 1 mm. in width, still persisted at the border, and the erythematous zone outside of this was about the same width as before. The base became slightly glossy upon drying. Figure 98 was taken at 5.30 p. m., March 16, 1918.

March 17, 1918, 9 p. m.—Total excavated area somewhat diminished. Border smoother. Floor not quite so deep. Total width of lesion was 15 mm.

March 21, 1918, 4 p. m. A brownish crust representing the necrotic base was beginning to loosen at the edges, where it was white and slightly desquamating. About this was a marked erythematous areola, 4 mm. wide. (Fig. 99.)

March 22, 1918, 9 a. m. During the night there was marked itching, the only pronounced subjective symptom so far noted. The crust loosened entirely and came off. Beneath the crust there was a small amount of thin purulent fluid. The erythematous zone was less marked. The base of the excavated area was again dry and covered with a yellowish-brown crust. The margin of the excavation was whitish, with edges slightly puckered. The central portion of the lesion measured 5 by 9 mm.



FIG. 96.—Mustard-gas lesion at 46 hours

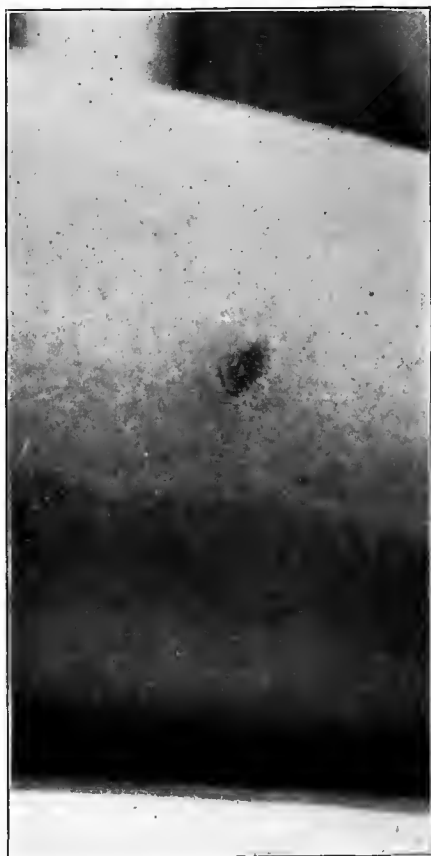


FIG. 97.—Mustard-gas lesion at 72 hours

March 30, 1918. Since March 22, the area of excavation had gradually become covered with a yellowish-brown crust which had become elevated nearly 2 mm. above the surrounding surface. The zone of erythema was fading, leaving a yellowish-brown pigmentation. The inner portion of this zone was shiny and somewhat puckered, and there were a few minute desquamating scales at the border of the dense crust. The entire width of the lesion, including the zone of pigmentation, was 3 cm., the reddened, somewhat shiny zone, was 2 to 3 mm. in width, the scaly desquamation about 1 mm., and the elevated crust 4 by 7 mm. (Fig. 100.)

April 1, 1918. The dark crust or scab became loose and came away leaving a white, dry, slightly granular area nearly flush with the surface of the skin. This measured 4 by 8 mm. (Fig. 101.)

May 1, 1918. Healing was now nearly complete, the lesion consisting of a thin scar, pinkish-white in the central portion and whiter, more opaque, at the margin, with very slight puckering. Around this was a brown pigmented areola. The whole area, however, was redder than normal skin. (Fig. 102.)

MICROSCOPIC APPEARANCES

The changes in human skin were studied microscopically from one-half hour up to four weeks, including the development of the vesicle and beginning eschar formation. As the lesions at one-half hour, 18 hours, and 36 hours represented three distinct stages, these will be described in detail.

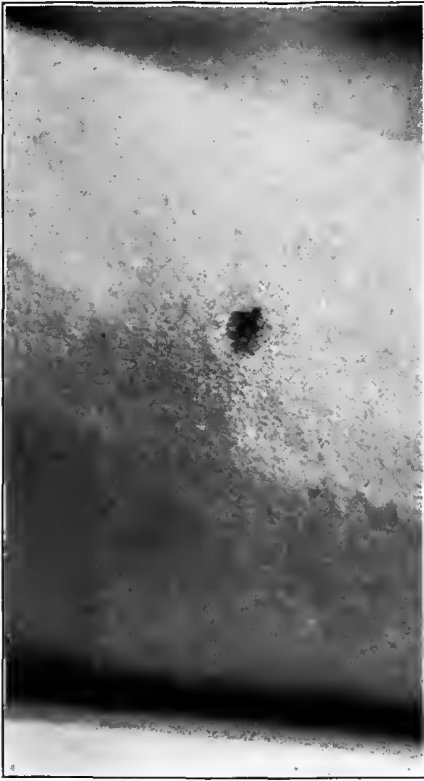


FIG. 98.—Mustard-gas lesion at four days

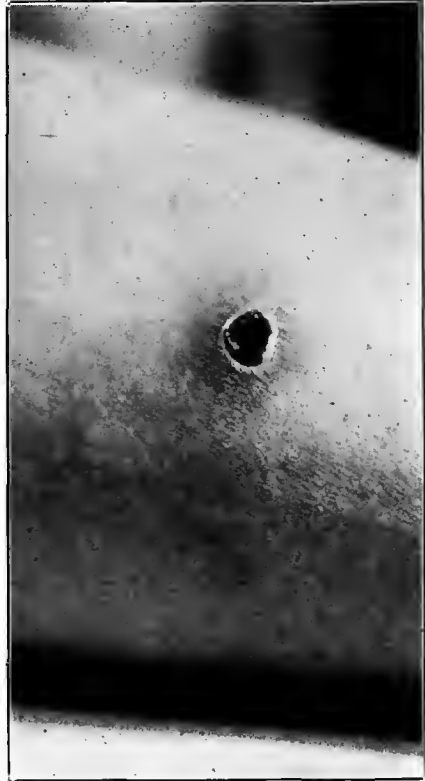


FIG. 99.—Mustard-gas lesion at nine days

LESION ONE-HALF HOUR AFTER APPLICATION

Epidermis.—The horny layer was relatively thicker than normal and split up into flat scales and layers, loosening readily from the stratum lucidum. The stratum lucidum had a slight brownish color. The granular layer was flattened; the cells drawn out parallel to the surface; the nuclei were pycnotic. The stratum germinativum was markedly shrunk, in many places only one-third to one-half as wide as normal, its nuclei pycnotic and the cytoplasm shrunk about the nuclei. Occasional vacuoles were found in the lowest layers, but the most marked change was the shrunk appearance of the whole epidermis, both cytoplasm and nuclei. At the border of the lesion the epidermis passed gradually into the normal condition.

Papillary layer of corium.—In the central part of the lesion the capillaries were contracted and contained but little blood. In scattered capillaries the

red blood cells were agglutinated and stained with eosin as bright red hyaline masses. Such agglutination thrombi, however, were not a common feature of the picture, and in the larger vessels thrombosis did not occur. The endothelium of the capillaries of the papillary layer showed marked pyknosis, caryorrhexis, and disintegration of the nuclear chromatin. Chromatin dust was found around many of these capillaries and also many of the connective-tissue cells of the upper portion of the papillary layer showed marked caryorrhexis. The cytoplasm of many of the endothelial cells of the capillaries was vacuolated, showing hydropic degeneration or edema. About these capillaries there

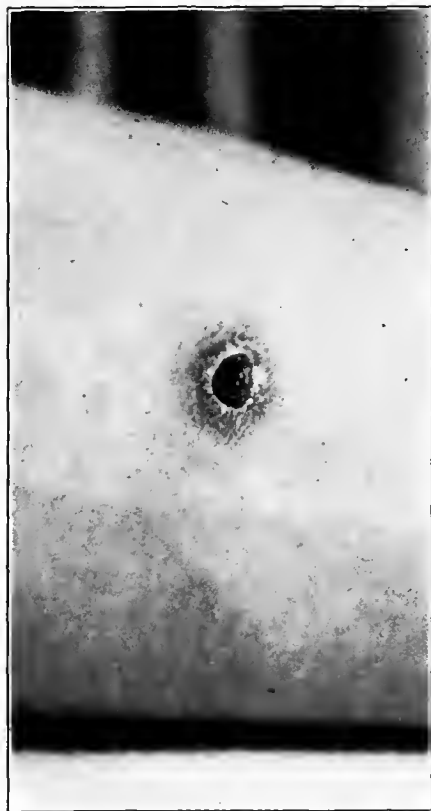


FIG. 100.—Mustard-gas lesion at 18 days

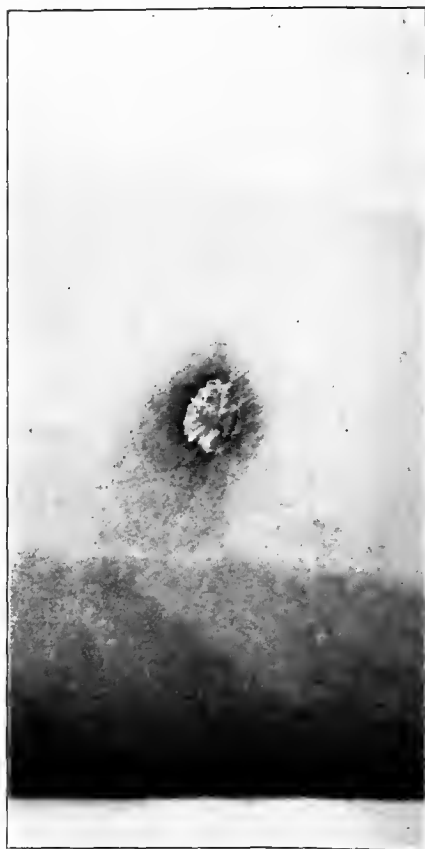


FIG. 101.—Mustard-gas lesion at 20 days

was a clear space due to a perivascular edema. Around some capillaries this was very marked. Many of the capillaries showed diapedesis of leucocytes along their course (fig. 104), but in the central part of the lesion there was practically no hemorrhage and the vessels were conspicuous for their contraction and anemia.

Corium proper.—The vessels running through the corium showed similar changes in their endothelium but there was little leucocytosis or white cell migration. The larger vessels contained more blood. No thromboses or hemorrhages were present. The lymphatics were dilated and the nerve trunks showed caryorrhectic nuclei and edema.

Hair follicles.—Along the hair follicles the squamous epithelium showed changes similar to those of the surface and the capillaries about the hair follicles also showed changes similar to those described above. In the neighborhood of the hair follicles the corium was affected more deeply than elsewhere, showing a distinct penetration through the hair follicles.

Sweat glands.—The epithelium of the sweat glands showed no apparent changes, although the vessels about them showed changes similar to those described above.

Sebaceous glands.—Shrinking and pycnosis of cells similar to that seen on the surface.

In the transition border there were small hemorrhages by diapedesis.

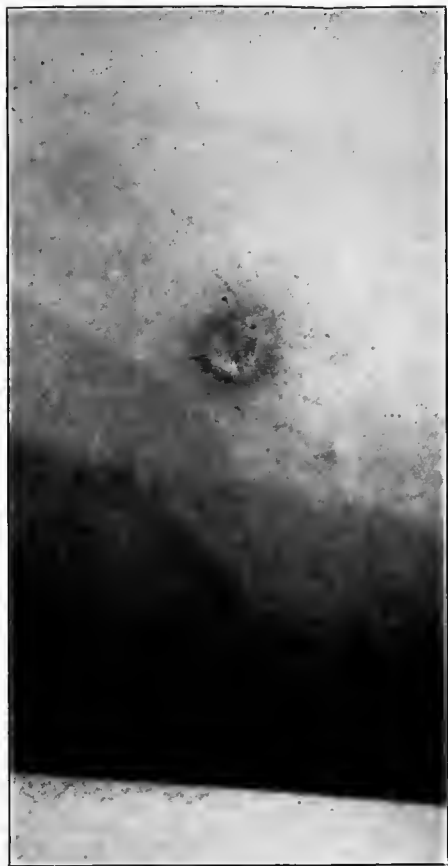


FIG. 102.—Mustard-gas lesion at 49 days

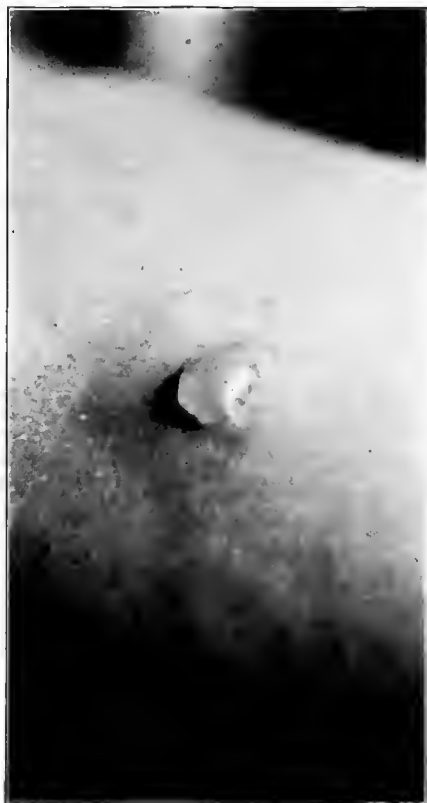


FIG. 103.—Typical mustard-gas vesicle about 20 hours after application

LESION 18 HOURS AFTER APPLICATION (FIGS. 105, 106, 107, AND 108)

Epidermis.—In the central part of the lesion there was a marked liquefaction and hydropic change in the cytoplasm of the epithelium. This varied greatly in degree. The horny layer was in part desquamated and loosened, the stratum lucidum was widened and more dense than normal and stained brownish-red. Over many of the papillae small vesicles had already formed, the majority of the epithelial cells having undergone liquefaction. In some places the epidermis was lifted from the papillae by the collection of fluid be-

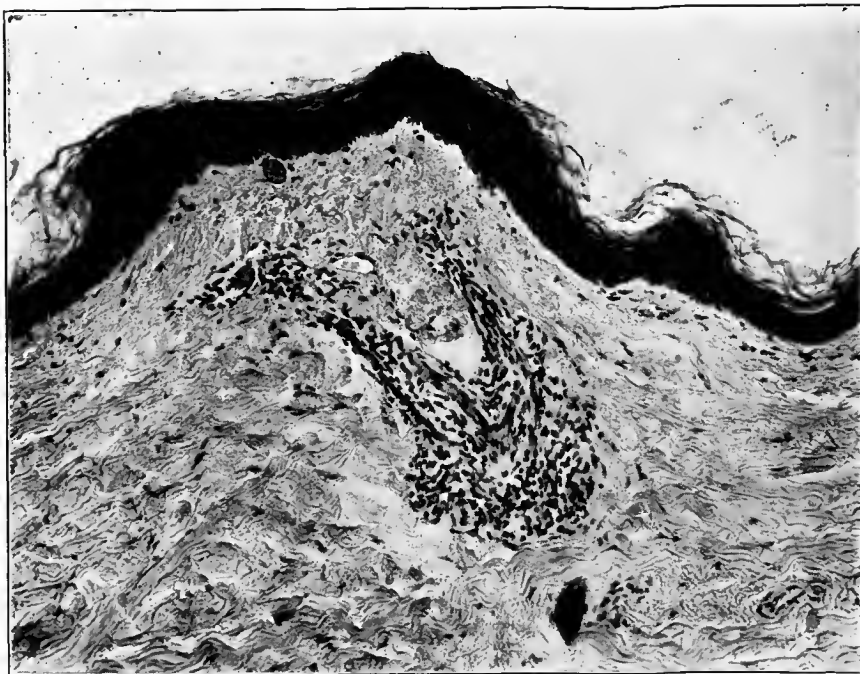


FIG. 104.—Lesion of human skin one-half hour after application of mustard gas

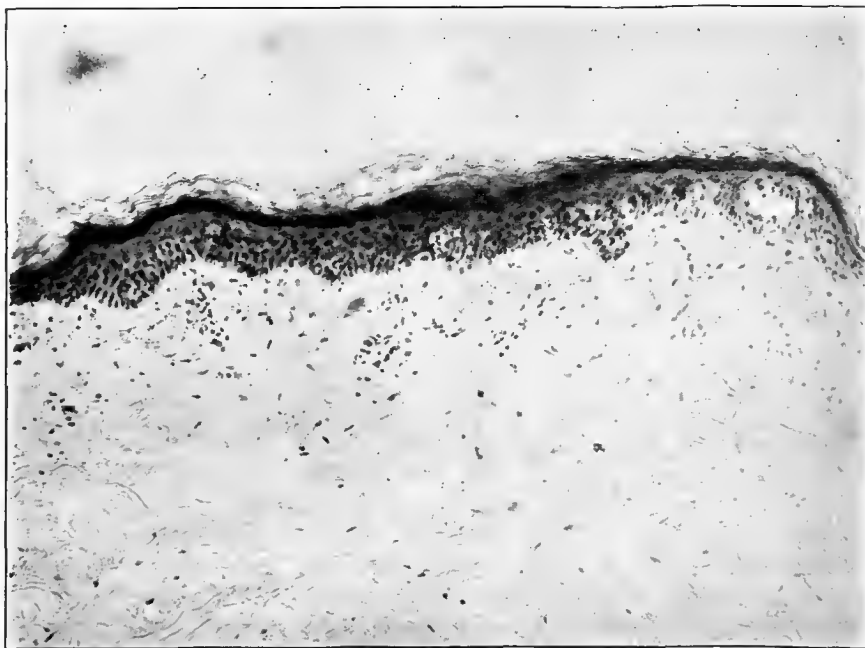


FIG. 105.—Human skin 18 hours after application of mustard gas. Transition between slightly damaged epithelium and epithelium showing hydropic degeneration. Early blister formation

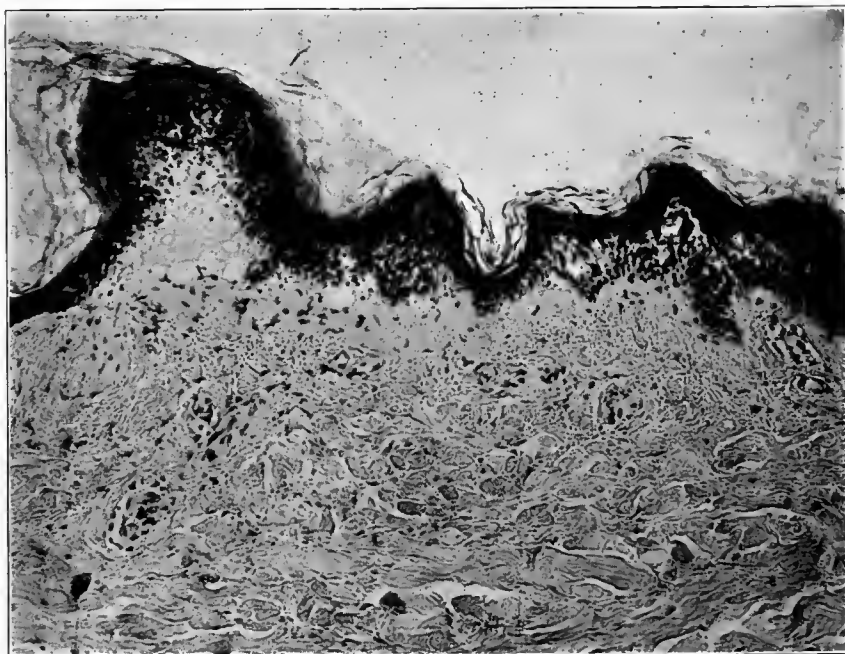


FIG. 106.—Human skin 18 hours after application of mustard gas. Early vesicle formation

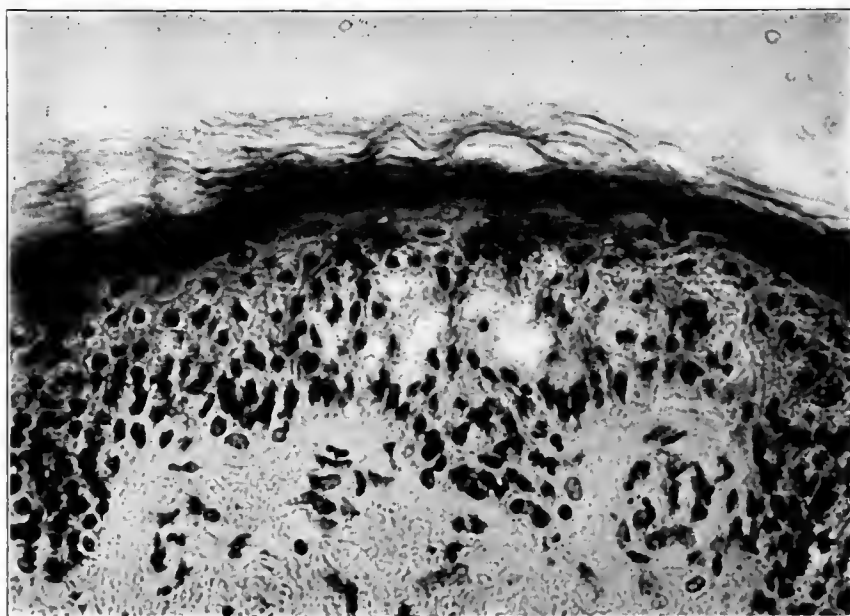


FIG. 107.—Human skin 18 hours after application of mustard gas. High-power view of hydropic change with early vesicle formation

neath it. The liquefaction of the cell cytoplasm extended deep down into the hair follicles and into the sebaceous glands. The stratum germinativum had lost its continuity in many places and the cells were completely necrotic.

Papillary layer of the corium.—The connective tissue was edematous, stained bluish, and contained many degenerating nuclei. There was an increase in the number of wandering cells and many of these showed caryorrhexis. Around all the capillaries there was a zone of edema and small-celled infiltration. Small hemorrhages by diapedesis were scattered through the papillary layer and upper portion of corium, particularly around the hair follicles.

Corium proper.—The blood vessels contained more blood than in the earlier lesion, particularly the deeper ones. The larger ones showed a marked congestion and the lymphatics were dilated with a lymph rich in albumin.

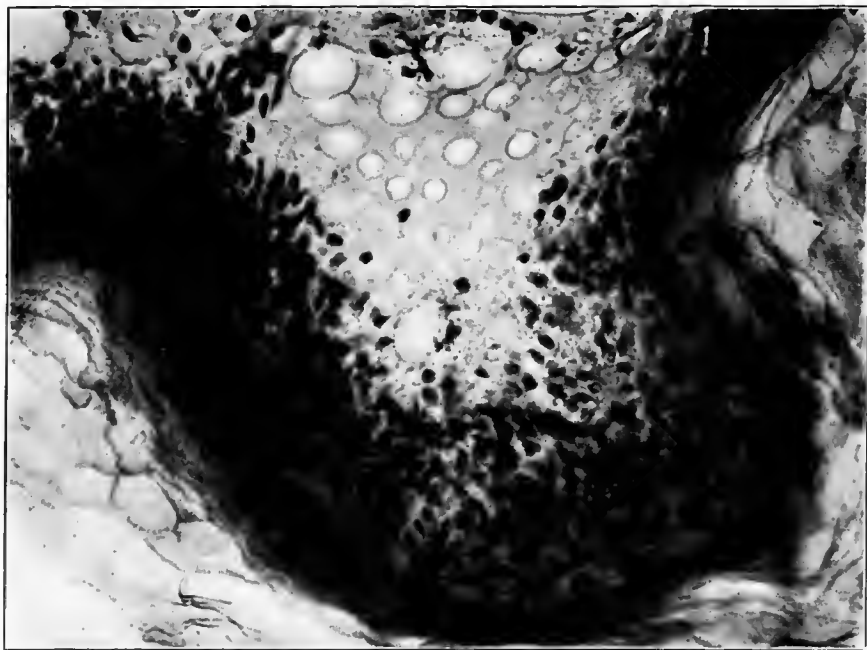


FIG. 108.—Human skin 18 hours after application of mustard gas. High-power view of small vesicles. Separation of epidermis from papillary layer

Around the hair follicles the edema, liquefactive changes, and hemorrhages were more marked than elsewhere. The sweat glands showed a marked edema of the interstitial connective tissue, congestion of the capillaries, leucocyte infiltration, and small hemorrhages by diapedesis. Some of the glands showed a marked necrosis of the epithelium but these changes varied greatly in degree.

Subcutaneous tissues.—The vessels were congested, lymphatics dilated, and there was edema of the adipose tissue. The vascular changes extended along the smaller capillaries even into the subcutaneous tissue.

LESION 36 HOURS AFTER APPLICATION (FIGS. 109 AND 110)

Epidermis.—The horny layer was more compact but ragged, and in many places infiltrated with leucocytes. The epidermis was nearly completely necrosed, in some places being lifted from the papillary layer. The remain-

ing nuclei were markedly pyknotic or fragmented. In many areas only the lowest layer of nuclei persisted. There were also collections of fluid between the horny layer and the portions of rete remaining.

Papillary layer.—The papillary layer showed marked edema, the capillaries were congested and there were many hemorrhages by diapedesis. The entire papillary layer was infiltrated with leucocytes, many of which showed earyorrhexis.

Corium.—There was a leucocyte infiltration throughout the entire corium, but less marked than in the papillary layer. It was most marked around the hair follicles and around the sebaceous glands and sweat glands. The congestion and edema were also most marked around these structures. Some of

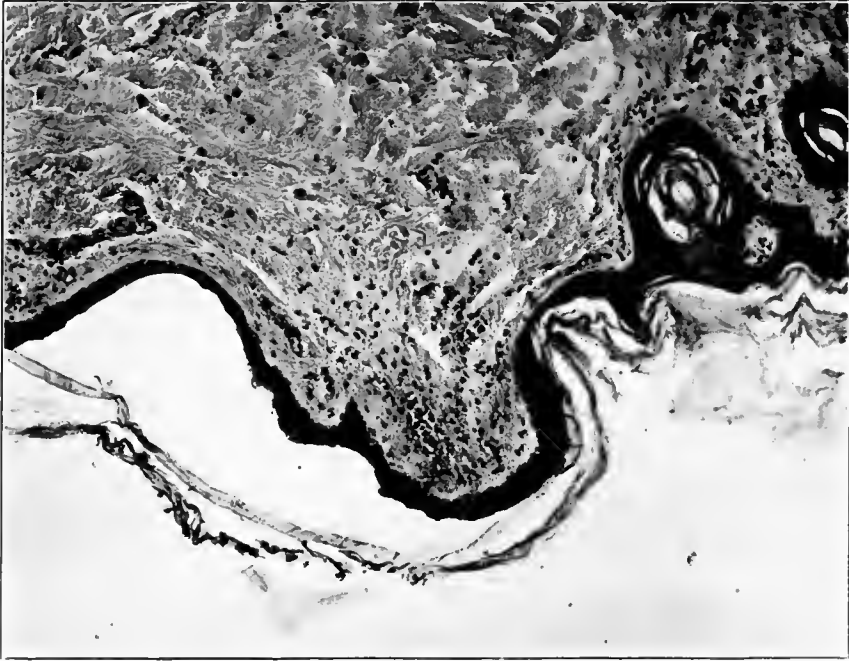


FIG. 109.—Human skin 36 hours after application of mustard-gas vesicle formation in epidermis and leucocyte infiltration of papillae

the smaller vessels showed marked necrosis of the wall with leucocyte infiltration and diapedesis. Scattered areas of edema and small-celled infiltration extended even into the subcutaneous tissue where the vessels were markedly congested.

LATER STAGES IN HUMAN SKIN

Inasmuch as the later stages in human skin paralleled those in the lower animals and as the specific differences between the action of mustard gas on human skin and on the skin of the rabbit, guinea pig, and cat existed only in the early stages, it seems advisable here to omit a more detailed description of these changes and to summarize them as follows:

1. About 40 to 50 hours after application, collapse of vesicles and progressive necrosis.
2. About 72 hours after application, progressive necrosis and beginning eschar formation.
3. Four to six days after application, necrosis completed, beginning separation of slough. Edema and hyperemia per-

sistent. The microscopic appearances of a droplet lesion on human skin at one week after application are shown in Figure 111. In the center the epidermis was completely necrosed and desquamated; the necrosis extended some distance into the corium; the surrounding area was intensely hyperemic; there was moderate edema, very little leucocyte infiltration, and no evidences of repair. 4. By the 19th day, complete separation of slough. Slow healing and scar formation. 5. For an indefinite period, congestion and pigmentation.

All of these descriptions apply to the effect of a standard drop of pure mustard gas in the absence of infection. The course naturally varied with the concentration, amount, time, and other factors. In very mild mustard-gas lesions, which appeared only as hyperemias, with intact epidermis, the microscopic examination might show a complete necrosis of the papillary layer of the corium with the exception of the chromatophores, which became larger,

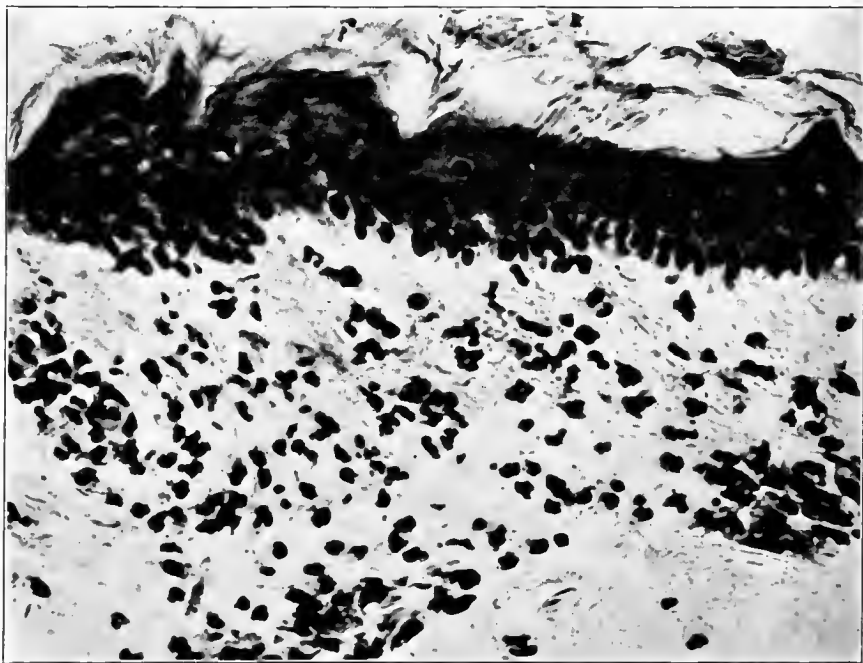


FIG. 110.—Human skin 36 hours after application of mustard gas. High-power view at border of lesion, showing changes in epidermis and leucocyte infiltration and edema of papillary layer

increased in number, and heavily pigmented. The pigmentation was due to melanin and not to blood pigment. This necrosis of the upper part of the corium explained the secondary production of vesicles through slight trauma.

ANIMAL EXPERIMENTS

The rabbit, guinea pig, and cat were employed for these experiments. The skin of the abdomen was shaved and standard drops were applied after the irritation from shaving had subsided. The character of the tissue lesion and the reaction in these animals proved, in the early stages, to be essentially different from the lesions in human skin. For the purpose of brevity and conciseness the protocols are condensed as below.

Rabbit.—Within two hours after application of the standard drop there developed a very marked edema, much larger than the area touched by the

drop of mustard gas. This edema was subcutaneous, appearing as a definite tumor mass, rather sharply circumscribed, over which the cuticle might be moved. The surface of the area appeared gray and cloudy, the skin losing its normal translucency and appearing as if it had been cooked. In some cases the blanching appeared to extend into the deeper portion of the skin. About this gray area there was but slight hyperemia. By the third day after the application the epidermis over the area had undergone complete necrosis and there was formed a slough without any vesicle formation. Vesicles were never observed in the rabbit. This slough was held on apparently by the hairs. It gradually became elevated, then separated and contracted, and might not be cast off for three or four weeks. When this slough disappeared, the lesion below was practically healed. The most striking features were the marked edema at the beginning, the persistence of this edema without vesicle formation, and the slow healing in the absence of infection.

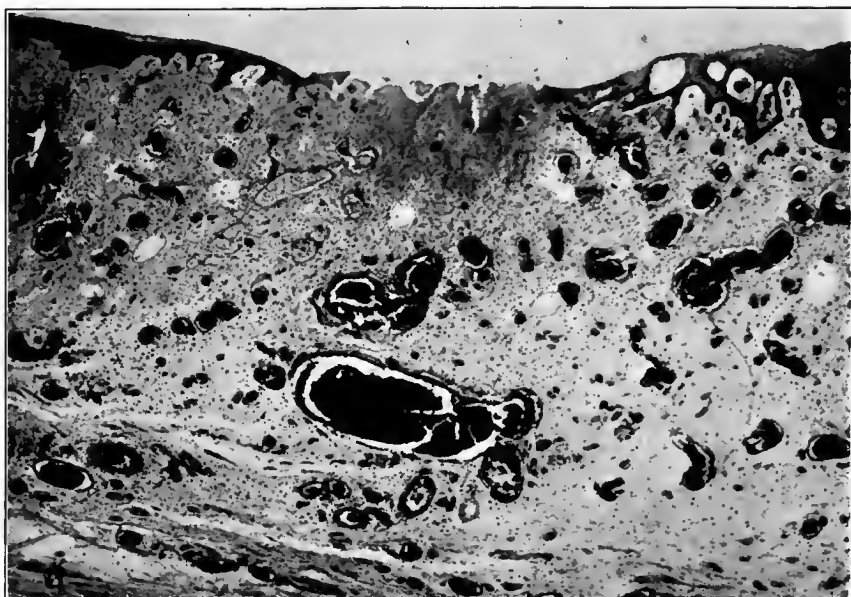


FIG. 111.—Droplet lesion of mustard gas on human skin seven days after application. Low-power view showing area of necrosis of epidermis and upper portion of corium, with intense hyperemia of the surrounding vessels. Moderate edema and very little small-celled infiltration

Various protective experiments were tried out, a number of substances being used to prevent the lesion or lessen its severity—washing with water, soap and water, lead acetate, lead acetate and silver nitrate, zinc oxide ointment, zinc oxide paste, bleaching powder, sodium sulphide, tincture of green soap, potassium permanganate. The application of most of these substances five minutes after the application of the mustard gas lessened the edema and rendered the lesion more diffuse but did not prevent necrosis. The use of potassium permanganate resulted in even greater edema than the untreated control while strong sodium sulphide solution was found to be disadvantageous because of the necrosis produced. (Figs. 112, 113, and 114.)

Guinea pig.—Practically identical results were obtained in the guinea pig with the standard drop of pure mustard gas; namely, within a few hours marked subcutaneous edema, followed in a few hours by necrosis of epidermis and papillary layer without vesicle formation and exhibiting very slow healing.

Cat.—The same results were obtained as for rabbits and guinea pigs. Subcutaneous edema without vesicle formation, followed by necrosis and slow healing.

MICROSCOPIC PATHOLOGY OF ANIMAL LESIONS

The changes observed in the development of the lesions in the rabbit, guinea pig, and cat were essentially the same.

STAGE OF MARKED EDEMA

The most striking feature of this stage was the intense edema which, although sharply localized to the subcutaneous tissue and fascia, extended also



FIG. 112.—Rabbit. Application of mustard gas at 11.30 a. m. Droplet used was slightly larger than the standard. Marked subcutaneous edema as seen at 4 p. m. on the same day

into the muscle of the abdominal wall. The connective-tissue fibrillæ were widely separated and the tissue spaces filled with a heavy albuminous precipitate staining deep pink with eosin. The muscle fibers of the abdominal wall were separated, and even in two hours there was a leucocytic infiltration into the muscle. The edema extended 0.5 to 1 cm. below the epidermis. The epidermis was shrunken, cells pyknotic, and in the central portion of the lesion completely necrotic. In the upper layer of the corium numerous degenerating nuclei were seen. The blood vessels showed degeneration of the endothelium

with small hemorrhages by diapedesis and leucocyte migration. Around each vessel there was an area of edema. There was, however, no vesicle formation in or beneath the epidermis as in the human cases. The changes were more uniformly diffuse in the animal than in the human skin and the depth



FIGURE 113.—Rabbit. Skin of belly shows results of four applications of standard drops of mustard gas. Above two areas of typical edema, the one on the rabbit's right untreated, the one to the left washed off in five minutes by water. The latter is more diffuse, larger in area, but less intense. Below, on the rabbit's right, an area washed after five minutes with soap containing an excess of free alkali. This area shows the least reaction. On the lower left is an area treated, after five minutes, with potassium permanganate. The reaction here is most marked.

of penetration greater. The localized penetration along the hair follicles, so prominent in the human skin, did not show in the animal skin, the greater number of hair follicles permitting a more uniform access of the liquid. There were no thromboses in the damaged area. The hemorrhages were relatively small

and, as in the human skin, the vessels in the immediate lesion were contracted and anemic. Around the borders of the lesion they showed marked congestion.

STAGE OF NECROSIS

The necrosis of the epidermis and of the underlying tissues steadily became more prominent because of the loss of nuclei in the epidermis and upper part of the corium of the central part of the lesion. By the fifth and sixth day after the application of the mustard gas the edema had subsided to a marked degree, and the central part of the lesion might be entirely without nuclei as far as the lower portion of the corium. It was bloodless, rather dry, and there



FIG. 114.—Rabbit. Two areas of mustard-gas application. Advanced eschar formation

was but little leucocyte infiltration. Surrounding this was a narrow zone of less marked necrosis and degeneration. This gradually became hyperemic and small hemorrhages by diapedesis took place from the damaged vessels. In this area there was a more marked infiltration of leucocytes but this rarely became diffuse, the leucocytes remaining collected in the neighborhood of the vessels. Outside of this zone the tissues were hyperemic, somewhat edematous, and showed an increased number of wandering cells for some distance.

STAGE OF ESCHAR FORMATION

There gradually began a separation of the completely necrotic tissue from the living. This eschar consisted of the dead epidermis and upper part of the

corium, sometimes as far down as the lower borders of the hair follicles. This dried, contracted, and became leathery, but was held in position by the hairs. There now developed in the neighboring living tissue a productive inflammation. The shrinking of the necrosed tissue and the demarcation, with the

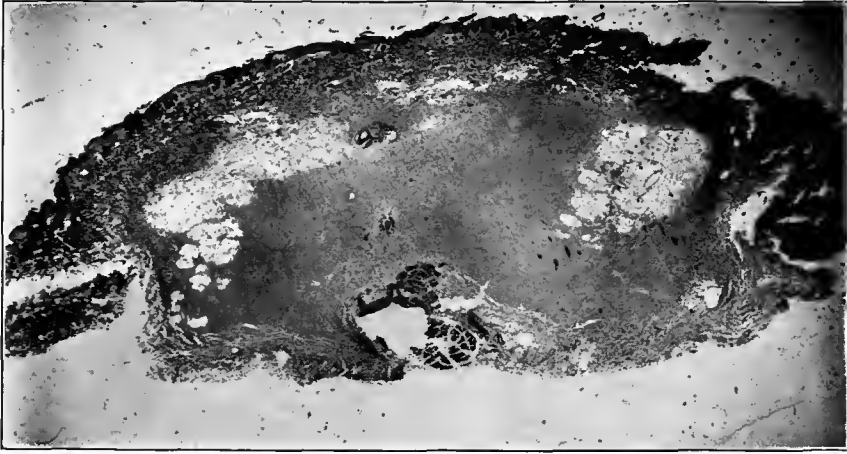


FIG. 115.—Rabbit. Low-power view of mustard-gas lesion in rabbit two hours after application. Extreme subcutaneous edema. Epidermis but slightly changed



FIG. 116.—Guinea pig. Low-power view of mustard-gas lesion five and one-half hours after application. Extreme subcutaneous edema. Epidermis necrosed in center of lesion

surrounding reparative inflammation, progressed very slowly until there was a regeneration of the epithelium beneath the eschar. The latter remained adherent, usually until complete repair had taken place. The repair of the epidermis occurred chiefly from the cells remaining in the hair follicles.

(For the histologic changes in animal tissues see figs. 115 to 126, inclusive.)

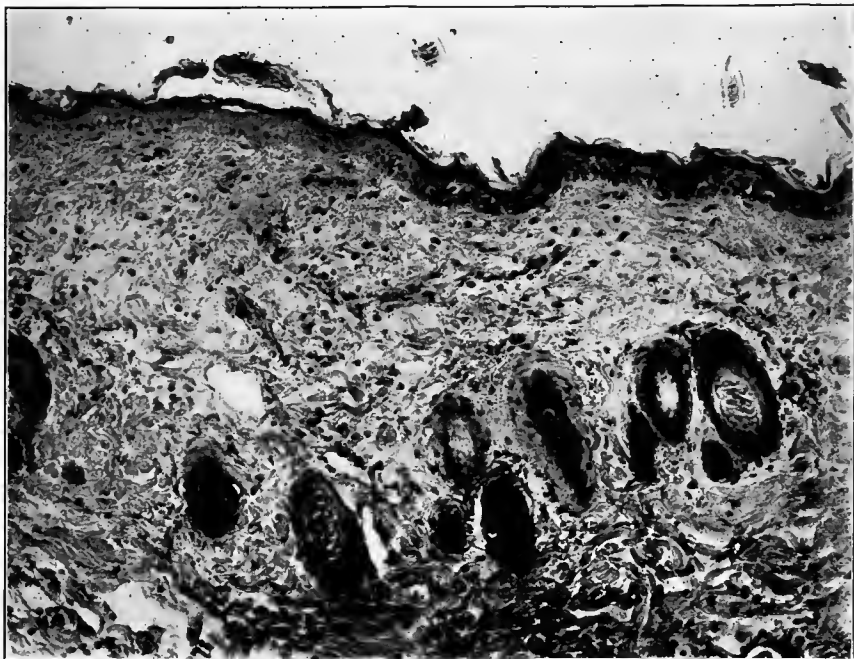


FIG. 117.—Border of lesion two hours after application of mustard gas. To the right of the middle, the epidermis is still living; to the left nearly completely necrosed, necrosis extending into the upper portion of the corium. Early edema

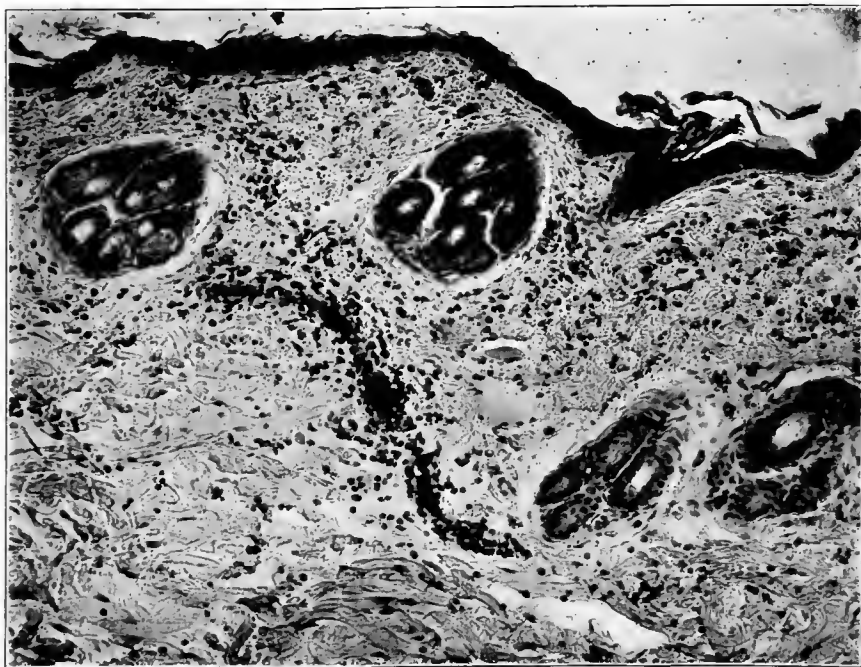


FIG. 118.—Rabbit. Two hours after application of mustard gas, changes in epidermis and corium. Marked vascular change with beginning migration of leucocytes. Small hemorrhages by diapedesis. Early edema

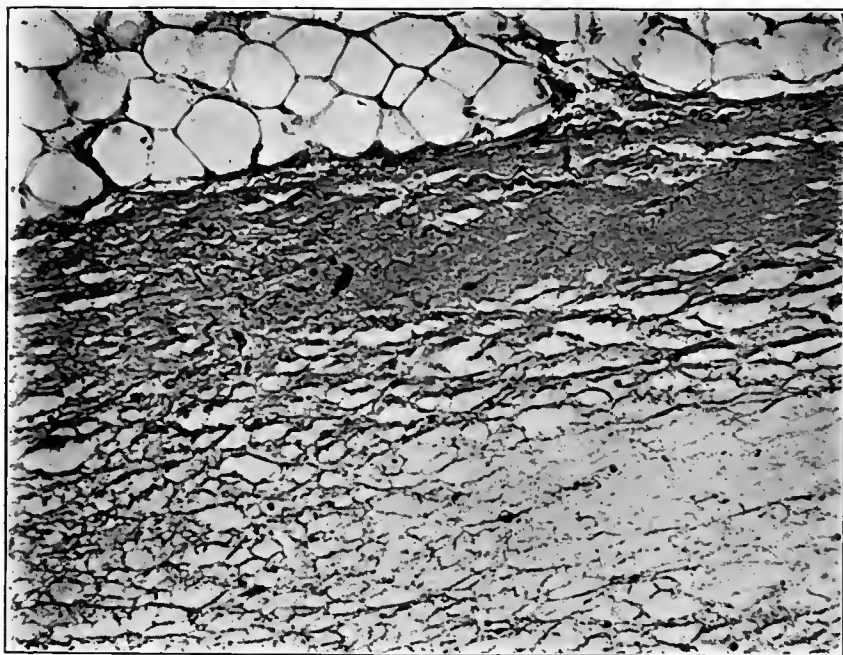


FIG. 119.—Guinea pig five and one-half hours after application of mustard gas to skin of abdomen. Deep subcutaneous edema

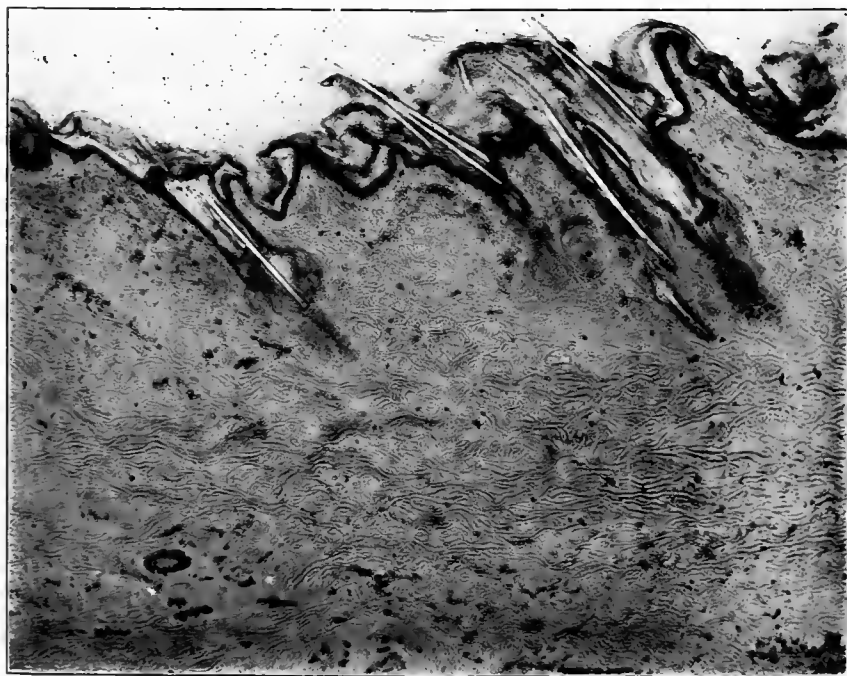


FIG. 120.—Rabbit. Six days after application of mustard gas. Treatment with zinc oxide paste five minutes after use of mustard gas. Center of lesion, complete necrosis of epidermis, hair follicles, and upper portion of corium extending even to the sweat glands. No reaction

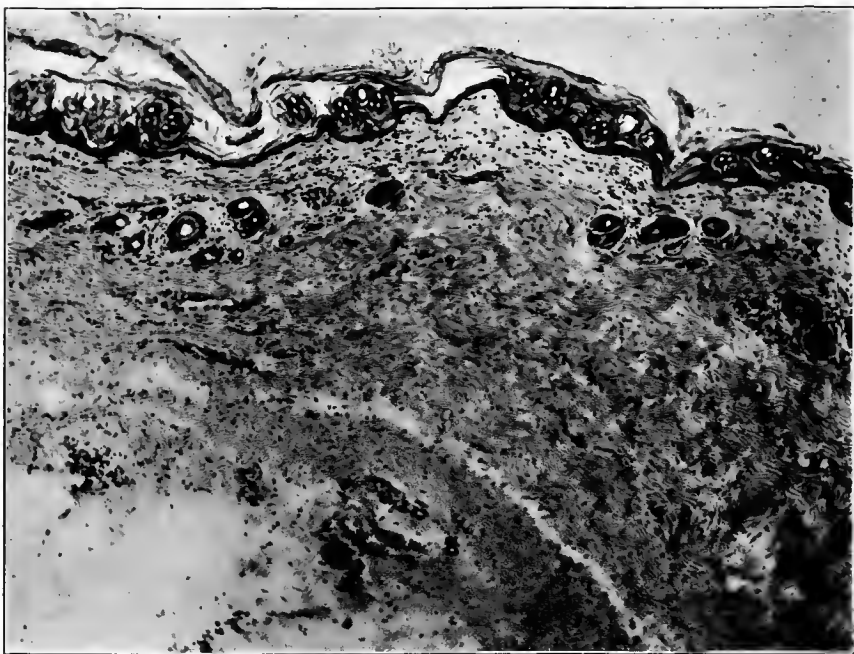


FIG. 121.—Rabbit. Six days after application of mustard gas. Treatment with zinc oxide paste five minutes after application. There was no edema stage. Epidermis is dead and there is a moderate inflammatory reaction in the corium. Reaction much less intense than in control

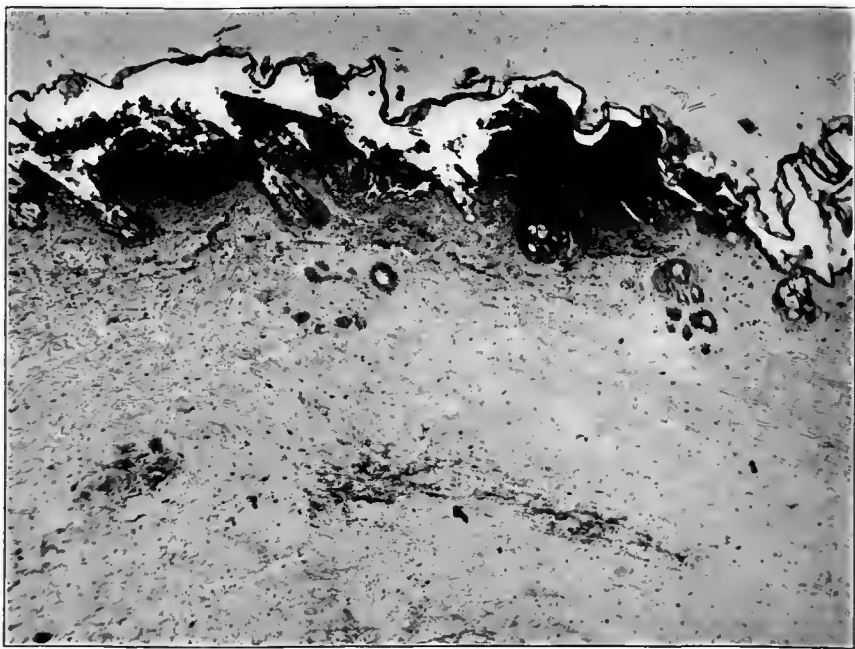


FIG. 122.—Rabbit. Six days after application of mustard gas. Treatment after five minutes with 2 per cent solution of silver nitrate and 5 per cent lead acetate. Primary edema was nearly completely controlled, but necrosis, six days later, is marked, extending deep into the corium, with more rapid separation of the slough



FIG. 123.—Rabbit. Periphery of same lesion as Figure 122. Area of less damage

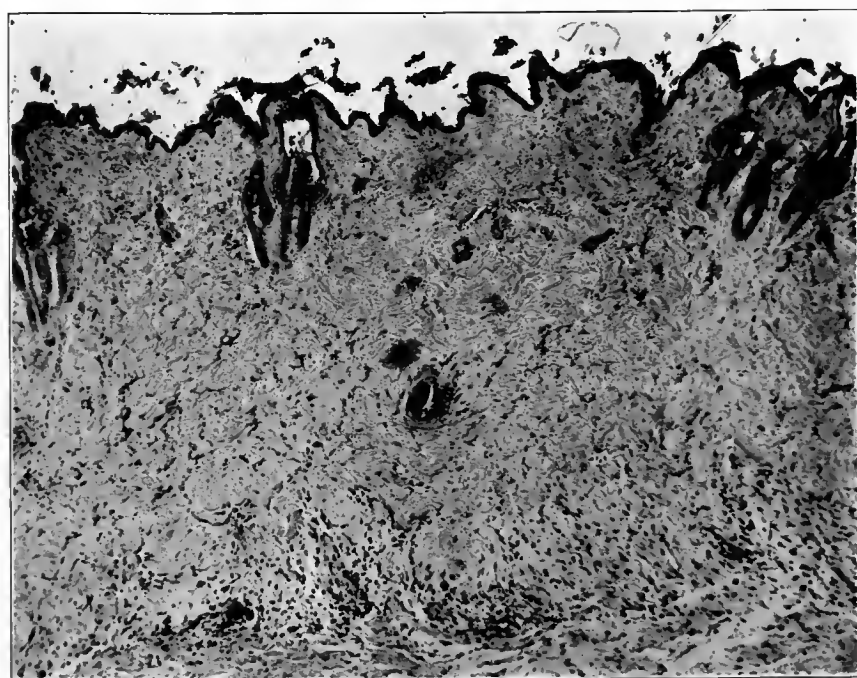


FIG. 124.—Rabbit. Six days after application of mustard gas, untreated. Border of lesion. Necrosis less marked. Beginning repair

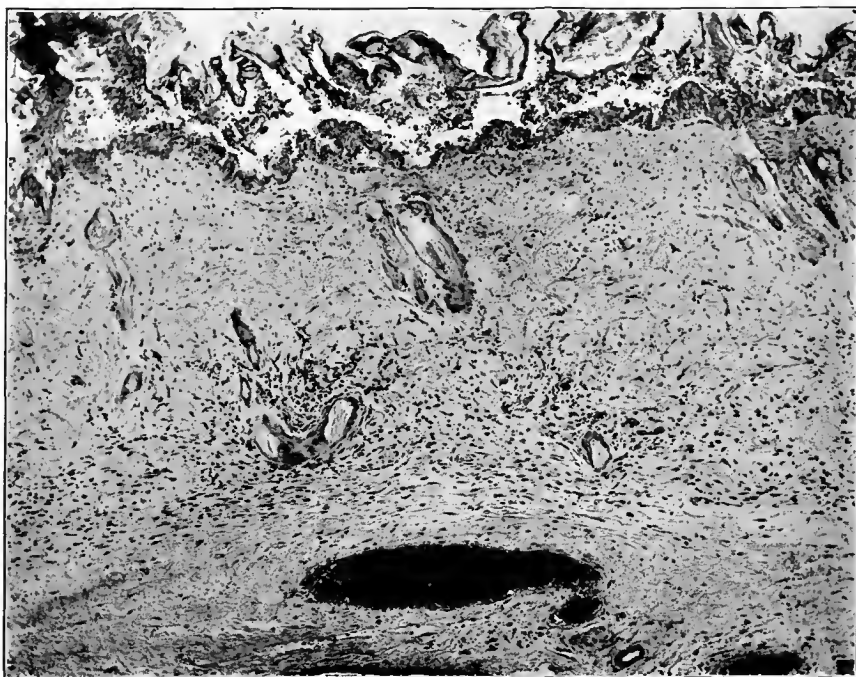


FIG. 125.—Rabbit. Six days after application, untreated. Intermediate zone. Separation of necrotic epidermis and papillary layer, with infiltration of leucocytes into the necrotic tissue. Fibroblastic proliferation in lower part of dermis, with regeneration of hair follicles. Intense congestion of subcutaneous vessels

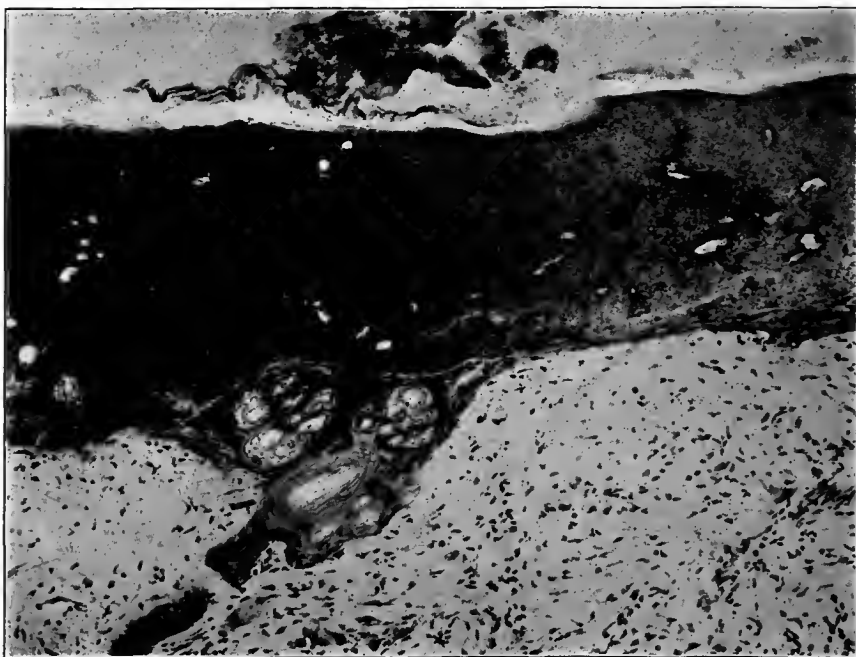


FIG. 126.—Rabbit. Six days after application, untreated. Adherent slough, representing the necrotic epidermis and upper portion of the corium, involving the hair follicles

CUTANEOUS LESIONS PRODUCED BY EXPOSURE TO MUSTARD GAS VAPOR HUMAN SKIN

Human skin exposed for varying periods of time to mild, medium, and strong concentrations of mustard gas developed lesions in proportion to the degree of concentration and time of exposure. These lesions were essentially the same as those produced by the direct application of the liquid gas. A third factor, that of susceptibility, appeared, however, to play a greater part in the cutaneous reaction to vapor, particularly to the mildest concentrations. This susceptibility was both a local and a general individual one. Local cutaneous susceptibility existed, particularly in the softer, more delicate areas of the skin, especially in the regions well supplied with sweat glands and exposed to friction. The skin of the genitalia and inner surfaces of thighs, although covered by clothing, was often the only part affected by the vapor. In other cases the skin between the fingers, flexor surfaces of elbows, axillæ, and eyelids was affected, while other portions of the epidermis might show very slight effects or none at all. Individual susceptibility appeared also to exert an influence in determining the severity of the reaction. Individuals with soft delicate skin, particularly those of the lymphatic constitution, showed an especial susceptibility, while those with thick, coarse, or pigmented skin showed less susceptibility. Other physical conditions affecting the skin during or immediately after the exposure undoubtedly played a large part in determining the individual effects of the exposure. Warm sweaty skin was more susceptible; pressure and friction upon the exposed areas were of the greatest importance in increasing the severity of the lesion. Slight rubbing would produce vesicles and eschar formation in parts exposed to vapor, when similarly exposed portions of the same area not rubbed would not pass beyond the hyperemic stage. Exposure of cutaneous areas to even the mildest vapors producing a barely recognizable hyperemia led to a remarkable tendency to pigmentation, much greater than that produced by exposure to sunlight or radioactivity. Frequent slight exposures might increase this pigmentation until the exposed individual became as dark as a negro. In many cases the pigmentation was very spotty. Exposures to very high dilutions (1:5,000,000) might produce itching of the scrotum and between the fingers without visible cutaneous lesions. Later pigmentation occurred in some instances.

The microscopic examination of cutaneous lesions resulting from exposure to mustard-gas vapor showed a pathology essentially the same as that resulting from the direct application of the liquid (figs. 127 to 138), in the stages of hyperemia, vesicle formation, eschar formation, and repair. The stage of pigmentation showed the production in the upper layers of the corium of large branching chromatophores that developed the pigment intracellularly. These cells were of endothelial or connective-tissue cell origin; never of epithelial. Later the cells of the rete came to contain the pigment also.

ANIMAL SKIN

Exposures of shaved areas of animal skin to vapor of mustard gas produced lesions essentially the same as those caused by direct application of the liquid mustard gas, varying only in degree of severity in proportion to the dura-

tion of exposure and concentration of the vapor. As with the direct application the lesions produced by the vapor in animal skin showed less tendency to vesicle formation than in the case of human skin, and the pigment formation was not a striking feature. Concentrations of 1:1,000,000 for a few minutes

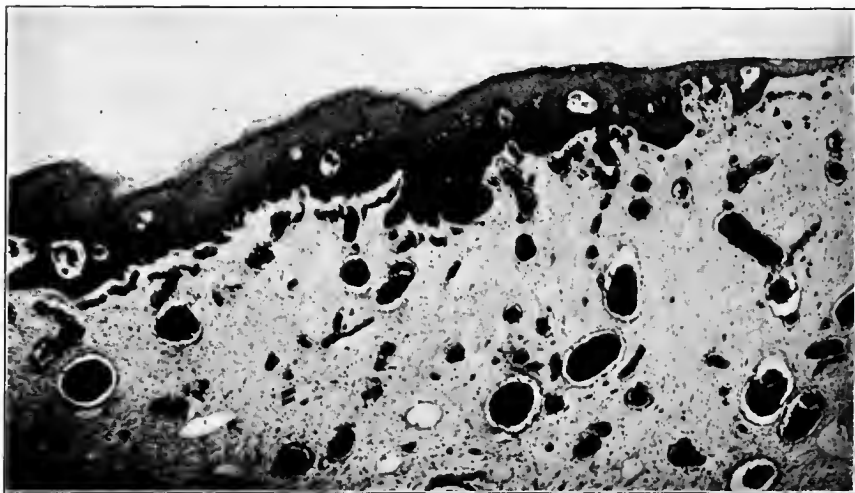


FIG. 127.—Section of skin of penis, eight days after exposure to strong concentration of mustard-gas vapor. Intense hyperemia

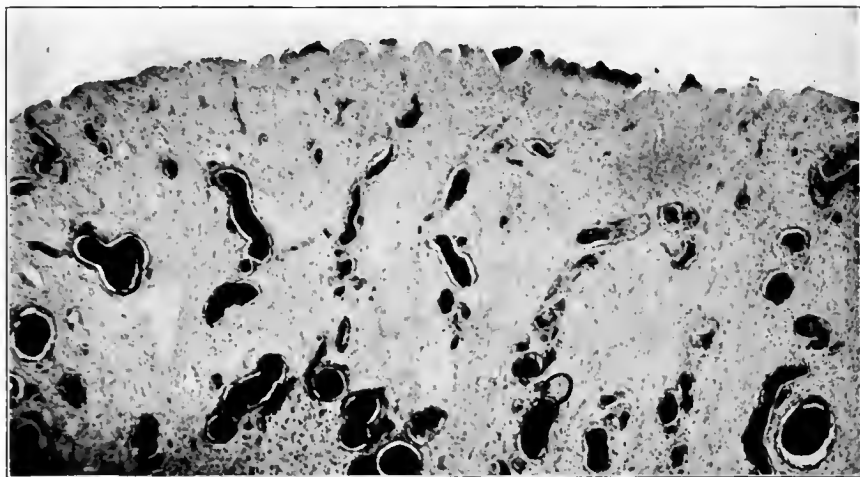


FIG. 128.—Section of skin of scrotum, from same individual as in Figure 127. Necrosis of epidermis; intense hyperemia

might produce in rabbits a hyperemia and edema lasting for several days. The microscopical picture of the vapor lesions in animals was essentially the same, varying only in degree, as that of the lesions produced by the liquid applications.



FIG. 129.—Human skin one week after exposure to strong concentration of mustard-gas vapor. Microscopically, the changes consist of increased cornification, pycnosis of the cells of the epidermis, and necrosis of the papillary layer of the corium. The only living cells in the upper portion of the corium are pigmented chromatophores

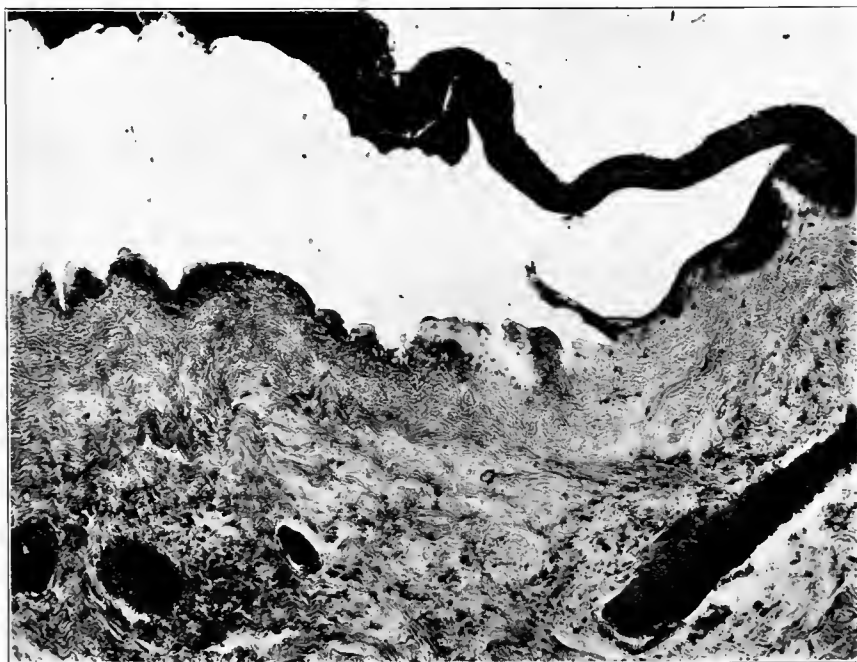


FIG. 130.—Human skin one week after exposure to strong concentration of mustard-gas vapor. Edge of large vesicle showing the necrosis of the upper portion of the corium, congestion of vessels, and separation of the epidermis

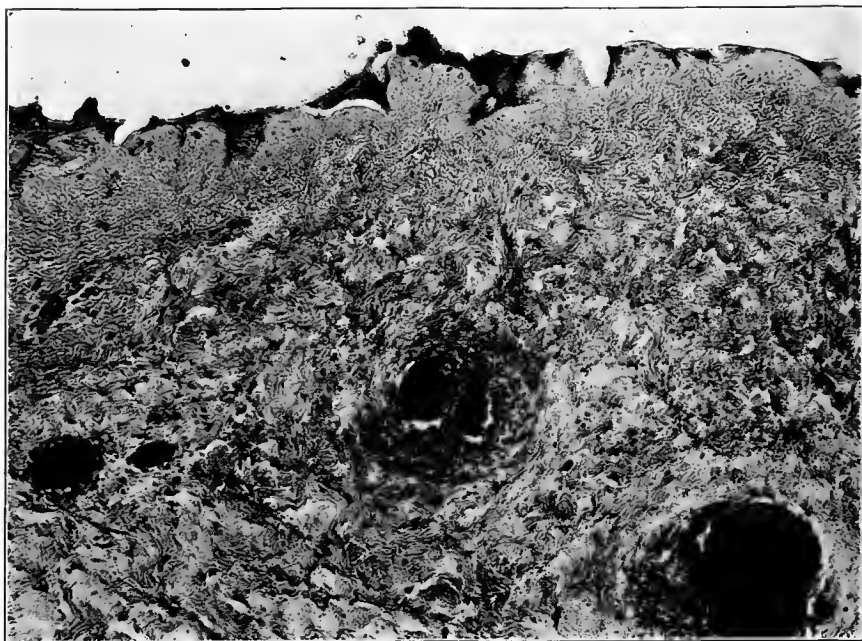


FIG. 131.—Section of skin from same case as Figure 130. Area of collapsed vesicles; necrosis of epidermis and corium; congestion of vessels

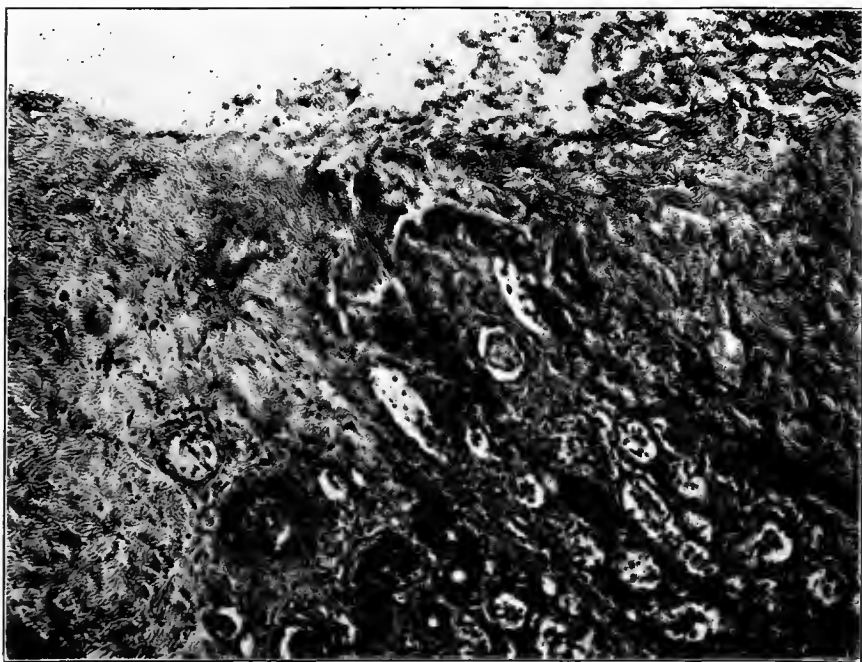


FIG. 132.—Skin from axilla of same patient as Figure 130. Necrosis of skin to the depth of the large sweat glands. These show also partial necrosis with some early regeneration

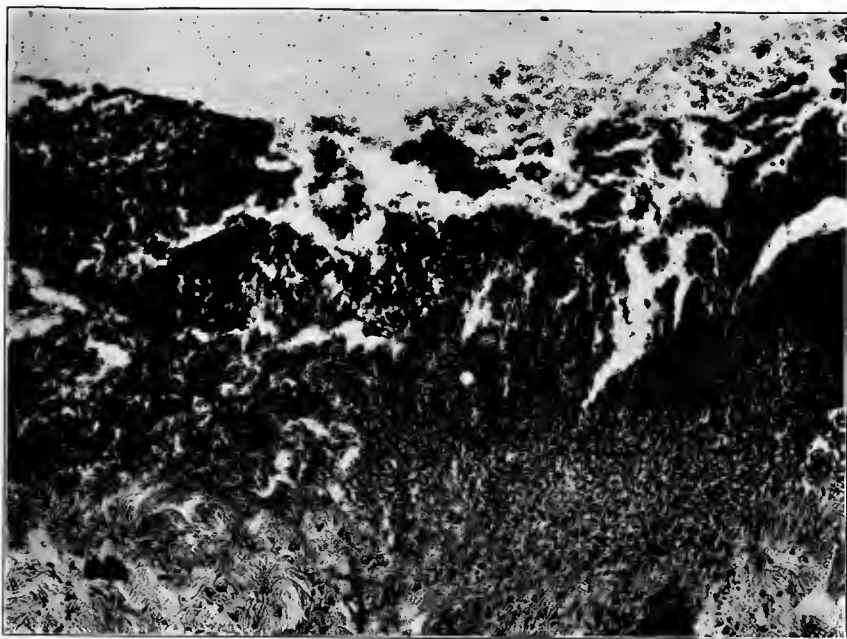


FIG. 133.—Infected gangrenous area from skin of back

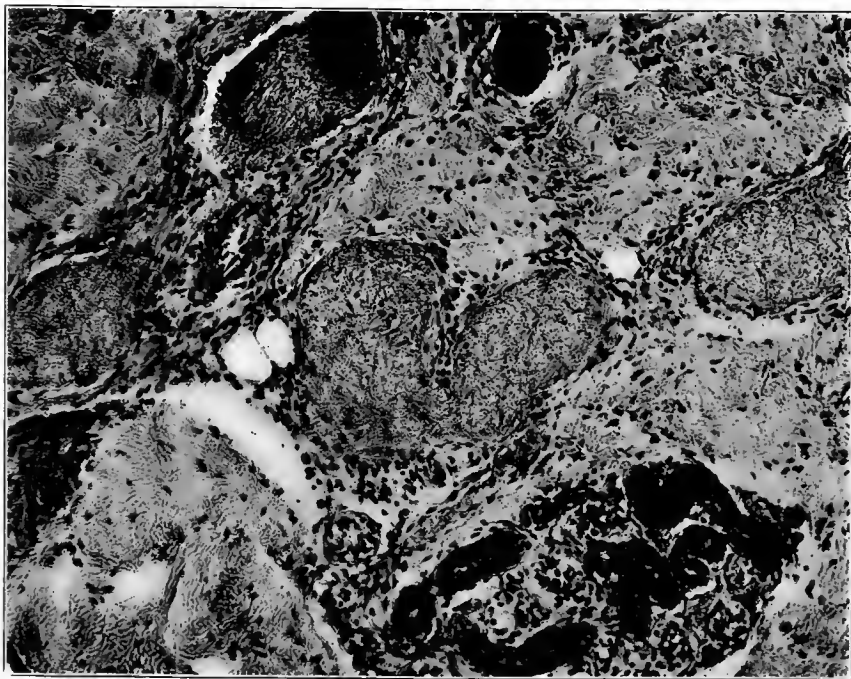


FIG. 134.—Section of corium from skin of same patient as Figure 130, showing dilated lymphatics filled with fibrin thrombi, in the lower portion of the corium. Some of these lymphatics contain partially hemolyzed red blood cells in small numbers



FIG. 135.—Microscopic section of eschar four weeks after exposure. Areas of regenerating epithelium from the sweat glands

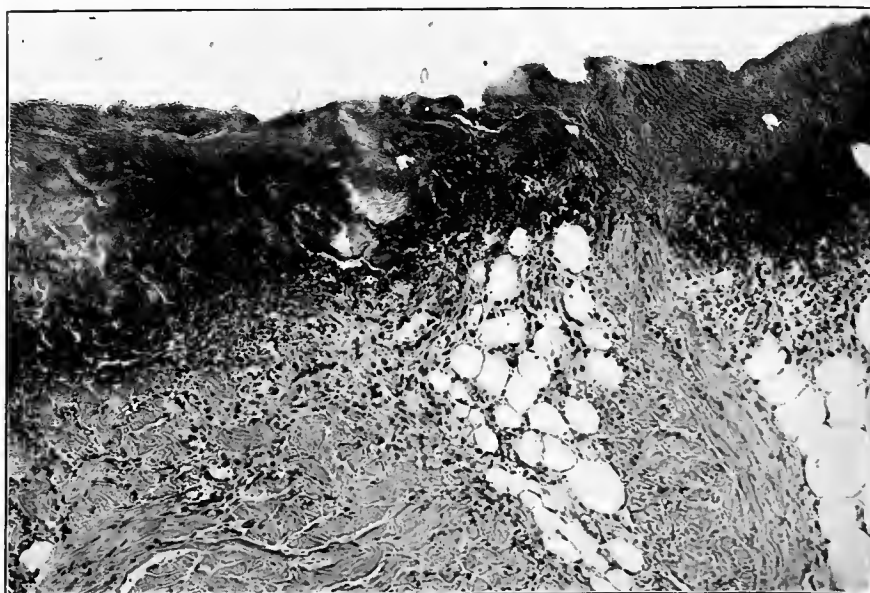


FIG. 136.—Microscopic appearance of mustard-gas decubitus four weeks after exposure. Destruction of tissue too great for regeneration. Necrosis extends below the level of the sweat glands



FIG. 137.—Photomicrograph of regenerating epidermis under the wet Dakin and saline method of treatment, four weeks after injury. Note the regeneration of the epithelium from the remains of the hair follicles and sweat glands

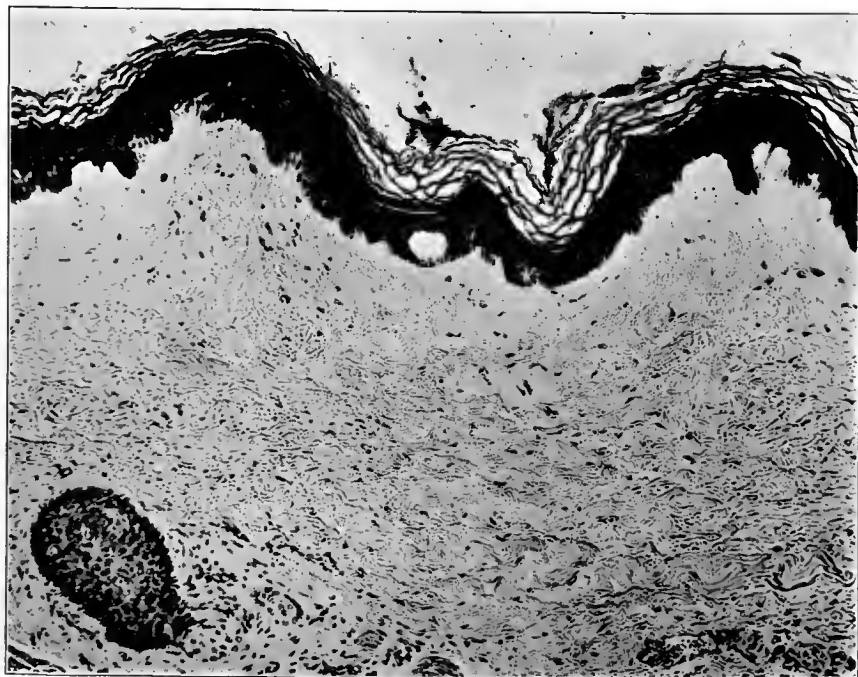


FIG. 138.—Completely healed mustard-gas lesion four weeks after injury treated 12 days with grease method, with increasing infection and gangrene. Under the wet Dakin and saline method infection was checked promptly and healing begun. Regeneration of epidermis from hair follicles and sweat glands

CLINICAL CASES

A large number of mustard gas lesions of the skin were observed in men engaged in the manufacture and handling of dichlorethylsulphide. Some of these cases were extremely severe, two of them terminating fatally. All possible degrees of cutaneous lesions were seen. From these the following seven cases are selected for illustration:^c

CASE 1.—Pvt. Mc. (Case 3, pp. 590, 610). Seen one week after an exposure for 40 minutes, in four shifts, to a strong concentration of mustard gas. Patient wore gas mask, rubber gloves, and rubber boots. One hour after exposure, after eating supper, he felt slightly nauseated, went out doors and began to feel very warm. Rolling up his sleeves he found his skin to be very red, and on opening his shirt his chest was also seen to be very red. He immediately started for the emergency room, but on the way became sicker and more nauseated. He then took a kerosene rub and a hot-water shower with soap, but as soon as the water struck him he vomited his supper. Then he took another shower, after which he vomited almost continuously for about five hours, altogether "about 100 times." At the same time his eyes began to smart intensely, and for three days he was in intense agony from the eye pain. He developed a very dry throat, a hacking cough, and difficulty in speaking. His severe symptoms lasted for three days, but his voice remained husky and he had a bronchial cough for some time. The erythema of the skin persisted but vesication and necrosis of the epidermis did not show for two days. When seen a week later, he presented the appearances seen in Figure 139. Over the entire area of erythema there was a branny desquamation of the epidermis and the skin appeared markedly pigmented, the pigmentation being deepest over the neck and forehead, region of the nipples, wrists, lower portion of abdomen, pubic region, and legs. In the hairiest part of the axillae the lesions showed eschar formation. Eschars were present also at the bends of the elbows, around the genitals, and in the popliteal spaces. The whole back desquamated. Over the back there were numerous small pustules. In the small of the back, just below the belt line, there were areas of necrosis covered with a greenish-gray crust. There were also minute pustules over the forearms and legs, varying in size from a pinhead to a pea. There was an odor of putrefaction about the genitals. The surface of the entire glans penis was necrotic; the skin of the penis was edematous, desquamating, and showed numerous necrotic hair follicles. The skin of the scrotum was edematous, desquamating, with a necrotic gangrenous surface, and exuding pus from all of the follicles. The inguinal lymph nodes on both sides were enlarged. The surfaces of contact between the genitals and the inner surface of the left thigh showed a deeper necrosis than elsewhere. Over the legs there was a large flaky exfoliation of the epidermis. The umbilicus was necrotic and infected. The ocular lesions are described on page 590.

CASE 2.—Pvt. M. (Case 5, p. 610). Exposed to the same strong concentration of mustard gas one-half hour in one shift. Thirty minutes after the end of the exposure he became nauseated and his eyes were irritated and burned. He took the routine kerosene rub and showers, but soon developed severe photophobia with symptoms of shock. Within a few hours entire body was erythematous. Vesication and desquamation began on the second day. When seen one week after the exposure his skin showed a general erythema and pigmentation except where protected by his rubber gloves, rubber boots, and belt. The skin of the neck was almost black; the horny layer had completely desquamated. Pigmentation was very marked over the forearms, hands, and abdomen, increasing toward the pubic region. The part of the face protected by the gas mask contrasted markedly with the deep black pigmentation outside of the borders of the mask. The back was erythematous and desquamating. The skin of the small of the back was almost black, except for the white belt line running across it. The buttocks showed intense erythema and desquamation. In the right gluteal fold there was an area of deeper necrosis. In the axillae, at the bends of the elbows, and around the genitals there were deep necrotic areas, exuding pus and giving off an odor of putrefaction. There was deep necrosis of the glans penis, of the scrotal skin, and of the contact surfaces of the genitals and skin of left thigh. There was a bilateral inguinal adenitis. There were numerous small pustules over the forearms and lower portion of the back.

^c These seven cases were studied with respect, also, to lesions of the respiratory and gastrointestinal tracts.



FIG. 139.—Photograph taken one week after 40 minutes' exposure to strong concentration of mustard-gas vapor. Treated with grease method during this time with increasing infection and gangrene of epidermis. Change of treatment to the wet Dakin's saline method effected prompt healing

CASE 3.—Pvt. H. (Case 7, p. 610). (Figs. 140 and 141.) Exposed 10 to 12 minutes in one shift to the same concentration of mustard gas as the above cases. First symptom was burning of the eyes; later mild shock, with vomiting; soreness of the throat and coryza. By the next morning had slight erythema over the body, most marked about the genitals. Vesication began on second day. When seen one week after exposure the face showed some pigmentation which was more marked in the neck, and the skin of the face and neck showed areas of desquamation with erythematous bases. The back was mottled with pigmented areas. Low on back the areas became confluent. Across the small of the back there was a sharply demarcated area which was protected by the belt. Over the pigmented areas there were flakes of desquamated epithelium. When these were removed an erythematous base appeared. The skin of the axillæ was very erythematous with areas of deep necrosis in the creases where the hair was thickest. There were also areas of deep necrosis in the bends of the elbows. Pigmented bands were present in the groin parallel with Poupart's ligament. The skin of the penis was erythematous without necrosis. The skin of the scrotum was necrotic throughout, with an odor of putrefaction. Areas of necrosis were present in the crotch. The buttocks were erythematous, pigmented, and desquamating. There were areas of necrosis about the anus. The skin of the popliteal spaces showed erythema, desquamation and slight necrosis.

CASE 4.—Pvt. E. (Case 6, p. 610). (Figs. 142 and 143.) Exposed 10 minutes in one shift at the same concentration as the others. He claimed to be especially susceptible to mustard gas because he had had frequent burns previously from slight exposures. He first noted irritation of the eyes and found that his left arm was red to the elbow. He took an American oil rub, after which he developed a general erythema. Vesication began on the second day. When seen a week later, the skin showed a general pigmentation except where protected by the gloves, boots, and gas mask. The pigmentation was the most marked over the face, thorax, and abdomen. The back was erythematous, with large areas of collapsed vesicles over the scapulae. The axillæ were erythematous, the skin desquamated, with deeper necrosis where the hairs were thickest in the folds. The deepest necroses on the upper part of the body were in the bends of the elbows. Wherever the skin had been rubbed over the bony prominences there were thick crusts of dead skin. Over the buttocks and the inner surface of the left thigh where the scrotum was in contact the skin was markedly erythematous, with branny desquamation over the entire body. The penis was markedly edematous and phimosed, with pus exuding from the meatus. The skin of the scrotum was completely necrosed and exfoliated. In the hair follicles there were numerous pustules. There were also small pustules over the forearms, shoulders, and back. Axillary lymph glands were enlarged. This patient had old mustard burn scars on his face, arms, and feet.

CASE 5.—Pvt. W. (Case 4, p. 610). (Figs. 144 and 145.) Exposed one-half hour in two or three shifts. Same concentration as in other cases. On coming from work he felt slightly ill and after eating supper was nauseated and vomited. He became very pale and showed severe shock. His throat was dry and sore and voice impaired. He had worn gas mask, rubber gloves, and rubber boots. He had also had mustard-gas burns of the hands previously. Showed general erythema a few hours after exposure. Vesication began on second day. When seen a week after exposure he was still in a state of severe shock and presented the signs of a diffuse bronchopneumonia. At this time his skin showed a generalized necrosis over the back, axillæ, chest, arms, abdomen, buttocks, groins, thighs, and popliteal spaces. The skin of the back exuded pus and there was a marked odor of gangrene over the entire surface, especially over the back. The chest and neck were deeply pigmented and the epidermis had exfoliated. Large patches of exfoliation were present over the chest and shoulders. The abdomen showed a marked line of demarcation corresponding to his belt. Everywhere a foul pus exuded from the necrotic surfaces. The genitals showed complete necrosis of the skin of the penis and scrotum, the surface being covered with a greenish gray slough, with numerous miliary abscesses corresponding to the hair follicles. The axillæ, buttocks, and popliteal spaces showed the deepest necrosis. The portion of the face covered by the gas mask showed a milder lesion. For several weeks this patient was at the point of death, but after changing the method of treatment from the grease to the Dakin's solution the infection was finally conquered and regeneration slowly took place. When seen several months afterwards, the patient was engaged in office work and his skin showed extensive areas of cicatrization resembling those of severe thermal burns.

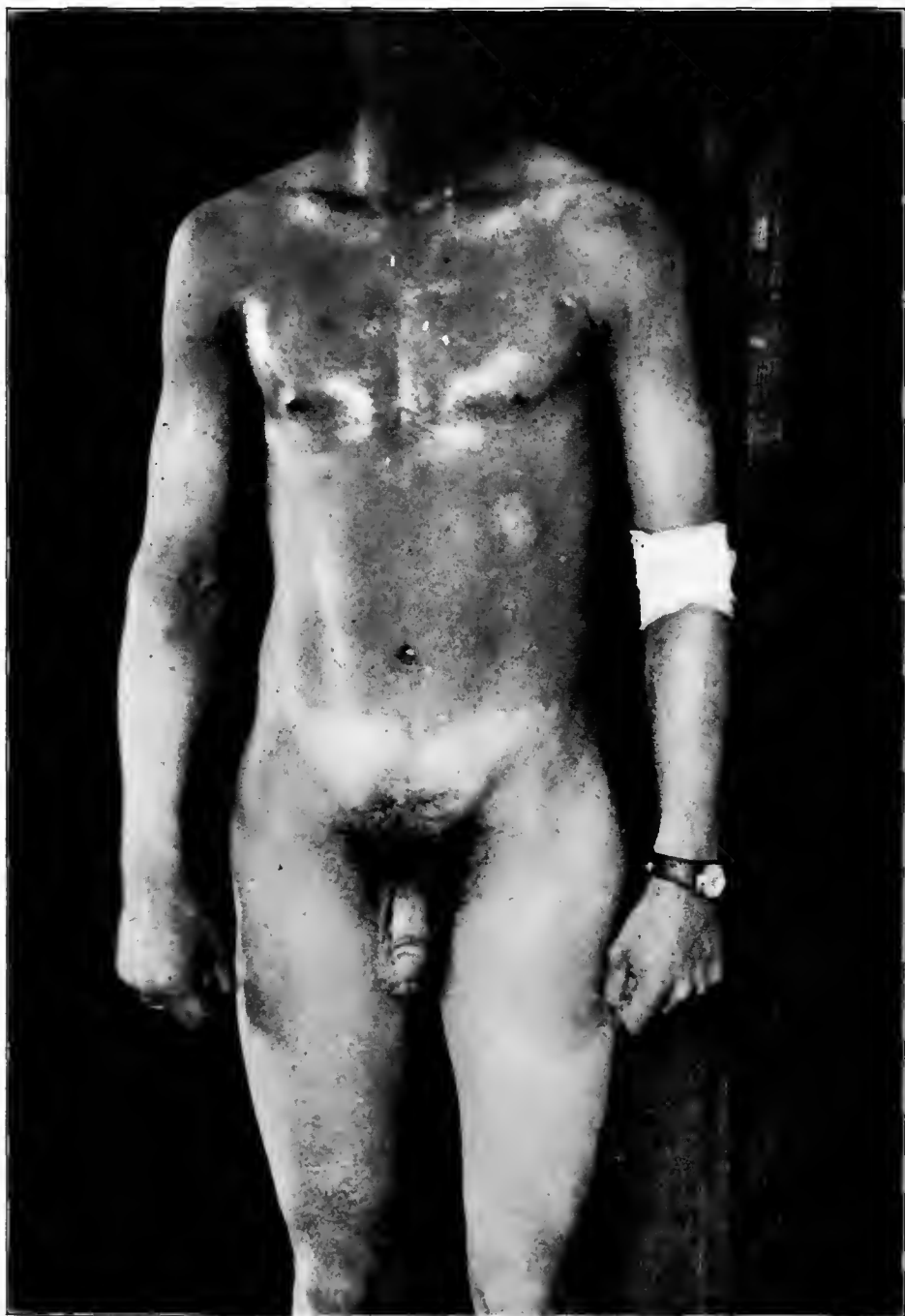


FIG. 140.—Diffuse erythema of the skin due to exposure for 10 to 12 minutes to strong concentration of mustard gas. Treated one week by the grease method, with increasing infection of the dead skin, particularly around the genitals and arms. Change of treatment to the wet Dakin and saline methods resulted in prompt healing



FIG. 141.—Rear view of same patient shown in Figure 140

CASE 6.—Pvt. Ha. (Case 1, p. 609.) Exposed one hour in two or three shifts at the same concentration. Almost immediately he became nauseated and pale, and vomited. He took a hot bath and kerosene rub, but quickly developed symptoms of severe shock. He vomited violently, had a severe diarrhea and extreme thirst. His face was pale but his body was very red. Two days later large vesicles developed over the back, chest, legs, and genitals. A condition of severe shock persisted. On the fourth day his temperature began to rise and an odor of putrefaction was noticed for the first time. The epidermis over his whole back was said to have been rubbed off at this time. By the fifth day the skin was discharging pus over the back, the patient became delirious, the pulse was rapid and thready, and the gangrenous condition of the skin increased. Death took place on the eleventh day. (For lesions of respiratory and gastrointestinal tracts see pp. 611, 620.) A description of the skin changes is given in full in the autopsy protocol on page 626.



FIG. 142.—Acute urethritis and phimosis due to mustard gas. One week after exposure

CASE 7.—Pvt. S. (Case 2, p. 610.) (Figs. 146, 147, and 148.) Exposed three-quarters of an hour in two or three shifts to the same concentration. On changing his clothes, he noticed that his head, face, and neck were very red except where the mask had covered the skin. He took the kerosene rub and bath, but soon became nauseated and developed symptoms of severe shock. At the same time an intensely painful conjunctivitis and a severe irritation of the entire skin developed. During the next three days vesicles developed over the entire body. These were opened and drained. Temperature began to rise on the fourth day. On the sixth day there was marked exfoliation of the epidermis. When seen a week after the exposure his skin was gangrenous and infected throughout and his condition was very bad. With the change of treatment to the Dakin's sponge bath and reduction of the infection his condition improved somewhat. At one time it was thought that he was out of danger, but his skin was almost com-

pletely exfoliated and large areas of decubitus developed over the back. Regeneration of the surface epithelium did not take place, and with the increasing decubitus the patient died four weeks after the exposure. An autopsy was refused, but a careful study was made of his skin and the localization of the lesions carefully determined, as in Figure 146. The nature of these lesions was as follows: The entire back showed a deep necrosis extending through the corium into the subcutaneous tissue in many places. In part, the necrotic surface was covered by a purulent exudate. Over the anterior surface of the body there were large irregular areas of deep necrosis, exuding pus. Between the areas of deep necrosis the epidermis was completely lost, the denuded surface was congested and the capillary tufts in the papillae of the epidermis could be easily seen. The portion of the face covered by the mask showed a deep erythema, pigmentation, and desquamation, with areas of necrosis on the lips and at the angles of the mouth. The skin of the genitals was gangrenous and there was a foul odor of putrefaction.



FIG. 143.—Buttocks of same patient as Figure 142

The surface was covered with a thick tenacious eschar, greenish-yellow or grayish in color. When this was removed, a purulent hemorrhagic base was exposed. Over the sacrum there was a large area of decubitus extending to the bone. (Figs. 147 and 148.)

Microscopic examination of the necrotic skin showed a complete necrosis of the epidermis and corium, with secondary infection, the necrosis in many places extending through the corium to the subcutaneous tissues. No evidences of regeneration were seen in these areas of deepest necrosis, but in those portions of the skin where the necrosis involved only the upper part of the corium areas of regenerating epithelium from the sweat glands were present. In the skin of the scrotum the regeneration of the hair follicles formed small solid masses of epithelium as large as a millet seed, which could be distinctly seen and felt through the skin. These had been regarded as follicular abscesses, but microscopic examination showed them to be regenerative areas of squamous epithelium.

SUMMARY OF CASES.

In addition to these cases, about 70 cases of local mustard-gas lesions of the skin of varying degrees, both in acute and chronic stages and presenting a great variety of clinical pictures, were seen.

As the result of observations on these cases the following conclusions were drawn:

1. Even after slight mustard-gas erythemas, particularly when these have been several times repeated, there develops a dry, desquamative eczema or dermatitis, particularly between the fingers and on the genitals, which may be mistaken for itch. This chronic lesion, otherwise trifling, is especially annoying for its constant itching. The genital lesions may be mistaken for venereal affections.



FIG. 144.—Photograph 1 week after one-half hour exposure to strong concentration of mustard gas. During this time treated by the grease method. Photograph shows very well the protection afforded by the tight belt. The more marked lesions in the axillæ, bends of the elbows, and genitals, and the large flaky character of the primary desquamation and the pigmentation are well shown

2. Slight mustard-gas lesions, not proceeding beyond the stages of erythema and pigmentation, may often be made to vesicate by slight trauma, such as rubbing, pressure, or by being struck. This phenomenon, which is analogous to Nikolsky's sign, has been misinterpreted as indicating a persistence of the mustard gas in the injured area with secondary action, or as a delayed reaction. It is due entirely to the lowered vitality or partial necrosis of the papillary layer of the dermis with the epidermis adherent, so that relatively slight injuries cause the epidermis to separate and form a vesicle.

3. It has been stated that the fluid of a mustard-gas vesicle when applied to uninjured areas of the epidermis will produce fresh lesions. This is not true. The fluid of these vesicles is absolutely without action upon either the skin or conjunctiva.

4. No specific susceptibility to mustard-gas lesions of the skin is acquired by repeated exposures. Healed mustard-gas lesions, like all other healed lesions, have a lower degree of vitality and are more susceptible to all forms of injury.



FIG. 145.—Back of patient shown in Figure 144

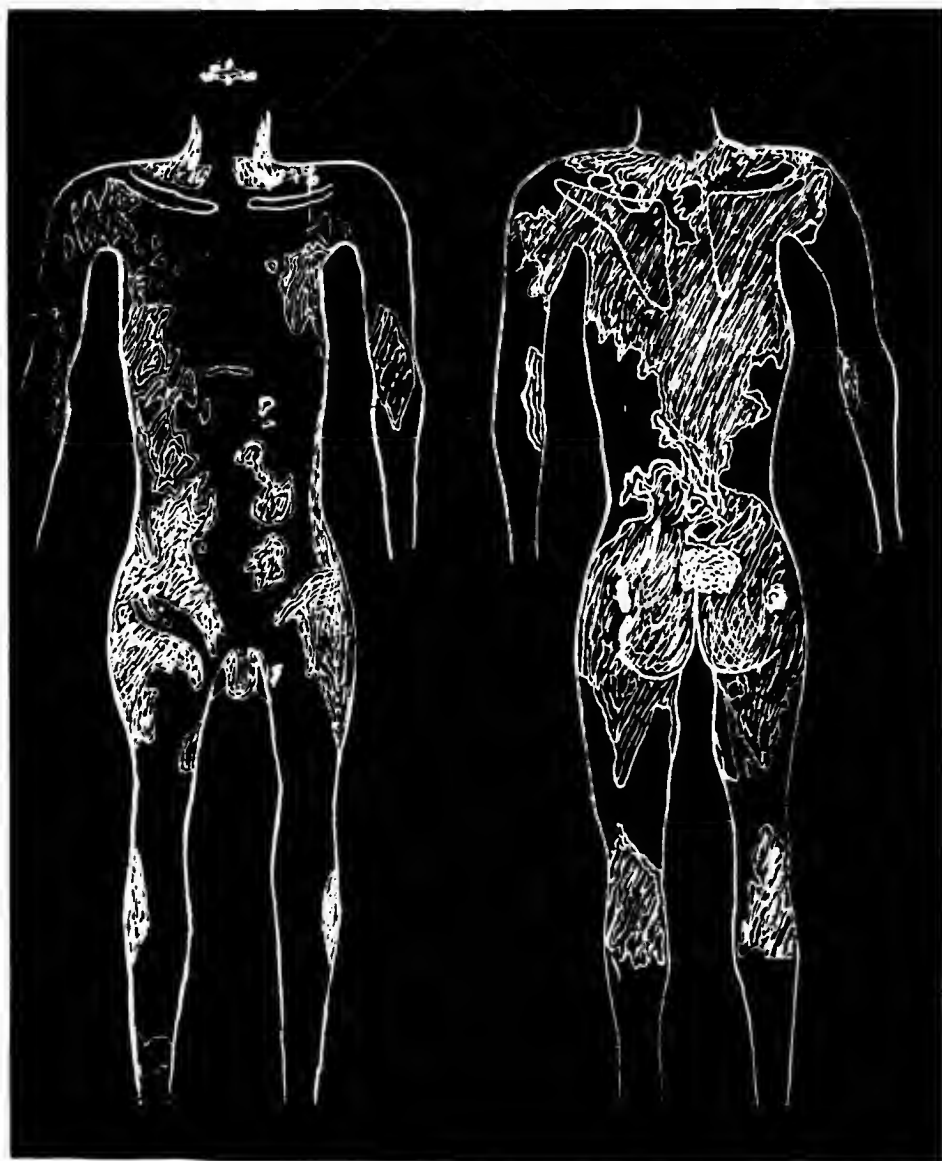


FIG. 146.—Diagram illustrating the distribution of mustard-gas eschars, four weeks after exposure to strong concentration of mustard gas. The hatched area represents the lesions



FIG. 147.—Mustard-gas lesions of back at one week



FIG. 148.—Skin lesions of mustard gassing one week after exposure

SUMMARY OF EXPERIMENTAL WORK AND CLINICAL OBSERVATIONS

1. Dichlorethylsulphide (mustard-gas) is an escharotic, specific in its action upon the epidermis and tissues of corium, particularly upon the endothelium of the vessels. The lesion may vary according to the concentration and period of exposure, presenting either a hyperemia, vesicle, or eschar. There is no essential difference between the lesions produced by direct application of liquid mustard gas and those caused by exposures to its vapors.

2. The lesion is a chemical burn unlike that produced by heat, electricity, or the ordinary corrosives such as sulphuric, nitric, and hydrochloric acids, or strong alkalis. Of all these agents, the effects are most closely allied to those of hydrochloric acid, but are much greater in intensity. It differs from a heat burn in the absence of thrombosis, in the greater degree of fluid exudation, in the greater moistness of the affected area and in the fact that the necrosis as shown by the loss of nuclei requires hours, or even days, for its complete development. The coagulated, shrunken and cooked appearance of the tissues in heat burns is not apparent in the tissues of mustard-gas burns.

3. The vessels in the affected area are severely damaged and collapsed and there is a local anemia in the earlier stages, with a marked fluid exudation and leucocyte migration. The process is nonhemorrhagic and nonthrombosing.

4. In clinical cases of general gassing with mustard gas, the skin is at first pale, then becomes erythematous within a few hours. With the development of the erythema there is usually intense shock with extreme nausea and vomiting. Vesication begins usually on the second day and progresses for several days, eschar formation appearing on the sixth or seventh day. The temperature usually does not rise until the development of escharization and secondary infection.

5. In man the necrosis of the epidermis is usually evident, microscopically, in two hours through the hydropic change in the epithelium and early vesicle formation. There is no deep edema. It is confined to the epidermis and to the papillary layer in the early stages.

6. In animals the intense and deep edema is most striking and altogether different from that seen in man. Vesicle formation was not noted in animals. The fluid from vesicles has no irritating property and can produce no secondary lesions.

7. The deep penetration of the smallest quantities applied to the surface is a most striking feature. There is an undoubted entrance through the hair follicles, sebaceous and sweat glands.

8. The slowly progressive development of the necrosis is a specific characteristic, the height of the necrosis being reached five to ten days after application. In this respect, also, there is a similarity to the X-ray burn. This may be explained, in part, by contraction and death of the vessels with resulting anemia in the affected area.

9. The painlessness of the lesion is also a marked characteristic. This may be explained by the edema and degeneration of the nerve endings in the affected portion.

10. Areas of the skin damaged by mustard gas may not show vesication or exfoliation unless they are subjected to pressure or rubbing. Slight trauma upon such damaged areas may produce vesicles or blebs some time after exposure. This phenomenon is analogous to Nikolsky's sign in pemphigus.

11. In none of the animals and in none of the clinical cases was there any conjunctivitis or irritation of the respiratory tract produced by local cutaneous applications. There is no evidence of metastasis from the local lesion, as claimed by both Meyer¹ and Haldane.⁸ The conjunctival and respiratory lesions are due alone to the direct action of mustard gas, and when animals are protected from the vapor no lesions in these organs will result, no matter how severe the skin burn.

12. Contrary to the statements of certain English and French observers, the admixture of water does not increase the escharotic action, but if the oil is immediately washed away the lesion is greatly reduced in intensity. Washing within two minutes with tincture of green soap may entirely prevent the lesion or result in only a slight hyperemia.

13. The lesions observed in the axillæ, between the fingers and toes, around the genitals, and between the thighs of men gassed in action are probably due to the greater moisture of these parts from perspiration and the resulting re-solution of the gas, as well as to the more abundant gland supply of these parts.

14. The slow healing is probably chiefly due to the vessel injury and the relatively slight leucocytic demarcating infiltration. In this respect the lesion is strikingly like an X-ray burn of the skin. Regeneration of the epidermis after complete necrosis takes place from the epithelium of the sebaceous and sweat glands. Marked pigmentation may persist for long periods. This pigmentation is due to the formation of many pigmented chromatophores in the upper portion of the corium. These findings present positive evidence for the production of melanin by connective tissue and endothelial cells. Chronic eczema, with desquamation and intense itching, is a frequent sequel to repeated slight mustard-gas burns.

OCULAR LESIONS

In spite of the fact that Victor Meyer, the discoverer of mustard gas, noted the conjunctival lesions in man and in experimental animals, the literature contains no reports of further investigations in this direction. The material presented below must therefore be regarded as opening up a new field in ophthalmic pathology.

EXPERIMENTAL LESIONS

METHOD OF APPLICATION

Application of dichlorethylsulphide to the conjunctiva was made in two ways: (1) By direct application of liquid dichlorethylsulphide; (2) by exposure to dichlorethylsulphide vapor. In order to secure results comparable to those obtained by direct application to the skin, as previously reported, an extensive series of animals was made use of, in which the liquid dichlorethylsulphide was applied directly to the center of the cornea by means of a fine pipette in uniform minute droplets determined to be about 0.0004 c. c. in size. The animal's lids were at once released and by its blinking the mustard-gas liquid was spread in the conjunctival sac. By using a uniform height of column of dichlorethylsulphide in the pipette the effort to maintain a standard size of droplet was quite successful. However, it is realized that slight variations in the amount applied were unavoidable. In another series, the animals were exposed to

dichlorethylsulphide vapor in varying concentrations and for varying times in a respiration chamber especially devised for the purpose. (See fig. 190.) Both pure and crude forms of mustard gas were employed.

SYMPTOMS AND GROSS PATHOLOGY

Although the objective symptomatology and gross pathology of the lesions produced by direct application of the liquid mustard gas and by exposure to the vapor were essentially similar in the two cases, there were slight differences depending entirely upon method of administration which makes it desirable to consider them separately.

DIRECT APPLICATION

Rabbit.—At once, upon application of a standard droplet (0.0004 c. c.) of dichlorethylsulphide to the center of the cornea, the rabbit blinked repeatedly but showed no other evidence of irritation for one or two minutes, when there was usually a period of rapid blinking and rubbing of the eye with the fore paws. At the same time there was a definite increase in lachrymation, but not to the point of epiphora. When at rest the eye might be held partly closed. Thereafter the rabbit showed but slight signs of irritation throughout the earlier stages, except that at long intervals the eye and nose were rubbed with the paws; the affected eye was opened as widely as the other, and lachrymation was moderately increased. Fifteen minutes after application there was beginning congestion of the vessels of the superior palpebral conjunctiva. At the same time there might be a slight decrease in the normal luster of the eye. The fluorescein test (see p. 567) was positive as early as 10 minutes. Thirty minutes after application there was increased lachrymation, and the congestion of the palpebral conjunctival vessels could be so marked that there was a pinkish reflex through the upper lid. These changes gradually increased during the next half hour.

At one hour the first evidences of edema appeared in the form of thickenings of the conjunctiva about 1 mm. in diameter. These occurred most frequently in the superior palpebral conjunctiva near the fornix and at the upper border of the nictitating membrane. These areas were so small and so translucent that they could scarcely be seen except with the aid of the loupe and electric illumination. From the second to the sixth hour there was a progressive increase in the conjunctival edema, the localized edematous thickenings extending and coalescing until the ring of swollen edematous conjunctiva so encroached upon the palpebral fissure that the sclera could not be made visible even by forced separation of the lids. The conjunctiva of the nictitating membrane shared in a marked degree in the formation of this edematous ring. The bulbar conjunctiva also showed a well-marked edema, a definite chemosis being noted about the fifth hour. Between the fifth and sixth hours after application the cornea began to show a faint clouding or haziness, especially in that portion of its lower half exposed in the palpebral fissure. The cornea was less lustrous than normal and when the surface was viewed under oblique illumination it was found to be somewhat roughened and irregular, indicating areas of destruction of the corneal epithelium. There was an increasing formation of seropurulent exudate. Photophobia gradually became more marked, the animal resisting all attempts to separate the lids. Lachrymation became excessive to the point of epiphora. The pupil reacted promptly to light.

From the sixth to the twelfth hour after application the edema of both palpebral and bulbar conjunctiva continued to increase. There was now a very definite chemosis. At eight hours the clouding of the cornea had reached such a degree that it might be properly described as porcelain-like because of its bluish-white opalescence. At this stage, likewise, there was noted an irregularly



FIG. 149.—Twenty-four hours after direct application of standard droplet of dichlorethylsulphide to cornea of right eye. Marked edema of lids and surrounding subcutaneous tissue

rounded area devoid of epithelium located in the mesial superior portion of the cornea. At ten hours the lids were found sealed by the accumulated sero-purulent exudate along their margins. This adhesion of the lids, first noted at this stage, was a constant feature until the gradual subsidence of the acute inflammatory process about the third week. Very minute subconjunctival hemorrhages were likewise first noted about the tenth hour.

From the twelfth to the twenty-fourth hour the picture remained fairly constant. There was a gradual increase in the edema which spread markedly into the periorbital tissues. (Figs. 149, 150, 151.) The stiffened lids stood out widely from the eyeball, and along the lid margins there was desquamation of the epithelium and other evidences of necrosis. The corneal opacity was still more marked, and in some instances there was a purulent fluid in the anterior chamber. This hypopyon was never in great degree in this stage.

During the second day the edema remained so marked that the eye could not be thoroughly examined except by excision. Eyes thus examined at 2-hour intervals showed a continuous progression in the lesion. The edema no longer continued to increase and in the 36-hour specimens a definite decrease was noted. In spite of this decrease the lids became even more indurated, indicating an increased cellular infiltration, and stood out far from the eyeball. The edges of the lids remained sealed unless forcibly separated, and in the pocket thus



FIG. 150.—Twenty-four hours after direct application of standard droplet of dichlorethylsulphide to cornea. Marked edema of lids, flecks of purulent exudate. The marked congestion of the conjunctival vessels is best seen in the bulging edematous mass of the superior palpebral conjunctiva



FIG. 151.—Twenty-four hours after direct application of standard droplet of crude mustard-gas liquid to the cornea. Extreme edema of conjunctiva, especially marked in upper lid and nictitating membrane. Seropurulent exudate.

formed thick purulent exudate accumulated. From the 44-hour stage on, this accumulation of thick purulent exudate became a very important feature. The denuded area upon the cornea increased in size and in practically all cases assumed a somewhat circular or elliptical form, occupying the greater part of the corneal surface but always approaching more nearly the inner quadrant of the limbus than the outer. The corneal opacity increased and frequently showed a curious distribution, similar to that which we have since learned has been described in human cases by Pissarello.⁹ This consisted of a greater degree of opacity in the lower half of the cornea terminating in a more opaque band or zone running horizontally through the cornea just below its transverse diameter. This was best seen in a 30-hour stage. The marginal lid changes became much more marked during that period.

The decrease in the edema continued through the third day, but was noted especially in the palpebral conjunctiva, while the bulbar conjunctiva, in contrast, exhibited a chemosis which appeared even more marked than hitherto.

The necrosis of the palpebral conjunctiva at the lid margins, and even of a zone on the dermal side of the lids, became more evident, for at that time there appeared numerous shallow ulcerations resulting from separation of the necrotic material.

On the fourth day the diminishing edema was followed by an increased congestion. More numerous and larger subconjunctival hemorrhages were frequently noted. These did not occur, however, in either such size or numbers as to permit the lesion to be characterized as hemorrhagic. The lids became increasingly sensitive to pressure so that the animals gave evidence of pain when an attempt was made to separate them more widely. In the earlier stages the photophobia seemed to be the feature that gave the animal distress. The upper lid, near the inner canthus, began to show a "kinking" or "ruffling" of the margin. This was a constant feature in the later stages. The marked seropurulent exudate continued to persist.



FIG. 152.—One week after direct application of standard droplet of dichlorethylsulphide to the cornea. Lids still somewhat edematous. They were sealed by a marked purulent exudate which adheres along the lid margins and to the adjacent hair. A marked purulent rhinitis, referable to involvement of the mucosa through the nasolacrimal duct, is evident

There were no marked changes in the lesions during the fifth day. The seropurulent exudate was unchanged. The "ruffling" of the upper lid was more marked and the lids were still indurated, standing far out from the eyeball.

In rabbits that had been repeatedly examined, thereby separating the lids and removing the accumulations of purulent and necrotic material, the exudate was less in amount and more serous on the sixth day. In animals allowed to remain with the eyelids sealed for days at a time, the seropurulent exudate persisted much longer and was, of course, much more destructive. At this time the necrotic lid hairs and the hairs of the face near the

inner canthus began to drop out, resulting in some instances in an extensive depilation.

On the seventh day there were no marked changes from those previously described. The depilation about the inner canthus and over the lids was more complete, and there was a beginning entropion of the upper lid which had the effect of drawing the stiff outstanding lid somewhat toward the eyeball. (Fig. 152.)

During the second week, the lids of eyes which had been frequently examined no longer became sealed between examinations, and the exudate decreased to a small amount of serous fluid carrying a few flakes of pus and necrotic tissue. The upper lid border showed a marked degree of "ruffling" or folding at the lid margin. This was accompanied by an irregularly distributed entropion. The lid margin itself became smooth, rounded, and devoid of lashes. The lower lid showed toward the end of the second week a marked ectropion, with the same smooth, rounded margin found on the upper lid. The periorbital depilation at times was very extensive. The corneal opacity was unchanged. The normal corneal curvature might be distorted by small, irregular, staphylomalike projections occurring most constantly inferiorly to-

ward the inner canthus. However, these on section were found to be thickenings of the damaged cornea and not areas of bulging. Hypopyon might be present. (Figs. 153, 154, 155.)

During the third and subsequent weeks the changes in the lesions were slowly progressive, demonstrating the sluggish character of the reparative process following injury with mustard gas. The "ruffling" of the upper lid border persisted and gradually became more exaggerated up to the eighth week, which terminated our period of observation. The ectropion of the lower lid also increased in degree, reaching in some cases an almost complete eversion. The margins of the lids were rounded, thickened, smooth, and glossy, having the appearance of scar tissue. (Figs. 156, 157, and 158.) From the fourth week on there was a progressive vascularization of the injured cornea. As the newly formed vessels traversed the limbus the usual differentiation between sclera and cornea became effaced. By the sixth week this process of organization became far advanced and the new-formed vessels might be traced to the central region



FIG. 153.—Two weeks after direct application of standard droplet of dichlorethylsulphide to the cornea. Marked reduction of edema. Much less purulent exudate. Indurated lids exhibit the characteristic "ruffling" and partial ectropion of the upper lid in the later stage and the smooth ectropion of the lower lid. The lower half of the cornea shows a marked clouding

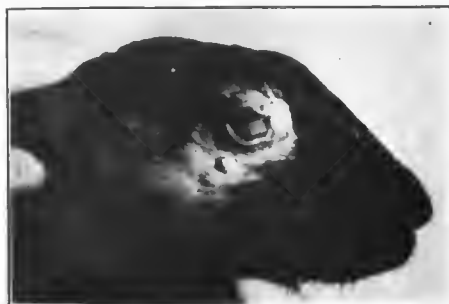


FIG. 154.—Two weeks after direct application of standard droplet of dichlorethylsulphide to the cornea. Marked depilation about the eye. Characteristic "ruffling" and ectropion of lower lid. The corneal cloudiness and lack of luster are very apparent, likewise the staphyloma in the lower half of the anterior quadrant

of the cornea as is clearly shown by Figure 159. The organization was grossly most evident in that portion of the cornea which showed the primary, porcelain-like cloudiness. When this involved the entire cornea, as in the case figured, there resulted, a complete opacity of the cornea, so that the iris and pupil could no longer be seen and blindness would be nearly, if not quite, complete. (Figs. 159, 160, 161.)

Dog.—Following the direct application of a standard droplet of liquid dichlorethylsulphide to the cornea of the dog, the changes ran closely parallel to those described above for the rabbit, and it seems unnecessary to describe them in detail. The earliest changes were identical. At the period, however, at which the rabbit's eye became sealed by the adhesion of the lid margins, the powerful orbicularis muscle of the dog prevented this occurrence. As a result there was never the empyema of the conjunctival sac that was found in the rabbit, and the exudate seemed to be less in amount. The congestion in the earlier stages was more marked, or at least more evident, than in the rabbit. The edema and the corneal necrosis were similar with the exception that the localization of the corneal opacity in the lower segment was never noted.

EXPOSURE TO MUSTARD-GAS VAPOR

Rabbit.—The symptoms and gross pathology produced by exposure to mustard-gas vapor varied with the concentration of the vapor and the length of exposure. In any case, they differed in degree, but not in kind, from those produced by the direct application of the liquid dichlorethylsulphide to the cornea and its immediate spread throughout the conjunctival sac by blinking. An exposure for 15 minutes to a concentration of approximately 1:20,000 was found to give results of about the same degree of severity as those produced by the standard droplet of liquid directly applied. The following notes are abstracted from a protocol of a rabbit subjected to mustard-gas vapor for that time and at that strength.



FIG. 155.—Two weeks after direct application of standard droplet of dichlorethylsulphide to cornea. Specimen obtained by excision of lids and orbital evisceration. Marked depilation especially at the inner canthus. Characteristic "ruffling" and entropion of upper lid. Corneal cloudiness

About five minutes after being placed in the gassing chamber the animal commenced to show signs of irritation, increased blinking, rubbing of the eyes and nose, and a change of position to bring the head as far as possible from the affluent opening by which the impregnated air was being introduced. Immediately after removal from the chamber the animal was quiet, but after a short interval continued to show increasing signs of irritation of the conjunctival and respiratory mucosa. These continued for the next few hours. At 5 hours after gassing a well-marked conjunctivitis was present. There was increased lachrymation, redness of the lid borders, beginning edema, and a marked photophobia. After 16 hours the signs and symptoms were all much more marked. The exudate had become somewhat mucopurulent; congestion of the lid borders and conjunctiva was increased and likewise the edema. The animal kept both

eyes closed because of the photophobia, which seemed much more marked. The edema reached its height about 24 hours after exposure, and a well-marked chemosis was then evident. All skin surfaces where the hair was thin showed a definite erythema. This was especially marked on the lids and convexity of the ears. A bilateral rhinitis, with abundant serous exudate also appeared at this time. The inflammatory changes of the upper respiratory tract were much worse at 36 hours, the wheezing respiration being distinctly audible at a distance. The eyes were sealed, and upon separation of the lids a large amount of thick purulent exudate appeared. The conjunctivæ were edematous and congested, and there were a few minute subconjunctival hemorrhages.

The lesions progressed slowly, as described for those produced by direct application. At 72 hours the clouding of the lower half of the cornea had appeared to a marked extent. The lids, having lost their edema to a considerable degree, remained stiff and stood out far from the eyeball, showing the first signs of the "ruffling" previously described. At 96 hours the lid borders began



FIG. 156.—Three weeks after direct application of standard droplet of dichlorethylsulphide to center of cornea. Same rabbit as Figure 154. Marked ectropion of lower lid. Porcelainlike cloudiness of the cornea most marked in the lower half



FIG. 157.—Three weeks after direct application of standard droplet of dichlorethylsulphide to cornea. Specimen obtained by excision of lids and evisceration of orbit. Anterior segment of globe in profile to show apparent staphyloma of cornea toward inner canthus. The corneal cloudiness is well shown

to show loss of the necrotic epithelium, with the formation of shallow ulcers. The corneal surface became roughened through loss of the epithelium, but no deeper ulceration could be demonstrated.

The lesions produced by this method have not been observed up to the stage of complete healing, as was done with those produced by direct application, but there are no apparent differences in the nature of the sluggish reparative processes in the two cases.

SUBCUTANEOUS INJECTION AND INGESTION OF MUSTARD GAS IN RELATION TO OCULAR LESIONS

An attempt was made to verify the statement of Victor Meyer that subcutaneous injection of dichlorethylsulphide determines the occurrence of a conjunctivitis, indicating not only a metastasis of the toxic substance through the blood stream, but also a selective affinity or special susceptibility of the conjunctiva. For this purpose we used a series of 4 albino rabbits, 2 hares,

and 2 dogs. The albino rabbits offered the greatest prospect of success, since in them the slightest conjunctival congestion could be readily seen. In the case of the rabbits and hares 1 minim of dichlorethylsulphide was given as a subcutaneous injection. In no instance was any trace of conjunctivitis or any other ocular change produced. The site of injection developed a waferlike induration which dried down to a deep-seated eschar. In every case there developed a foul diarrhea, to which most of the animals succumbed on about the sixth day. One large dog received 4 minims subcutaneously. There was no conjunctivitis, but a severe diarrhea developed, and death occurred on the fourth day. Another dog was fed 4 minims in meat. Severe burns of the



FIG. 158.—Rabbits' eye at 4 weeks after direct application of standard droplet of dichlorethylsulphide to cornea

mouth and upper alimentary tract were produced, but there was no conjunctivitis. These lesions in the gastrointestinal tract will be considered more fully later in this chapter. Attempts to produce conjunctivitis or other eye lesions by intravenous injection also failed; although this fact has little weight since death occurred too soon to permit the development of marked changes.

RELATIONS OF PANOPHTHALMITIS TO MUSTARD-GAS LESIONS

In the ocular lesions produced by the standard droplet and by exposure to a vapor concentration of 1:20,000 for 15 minutes, with ordinary care given to the eyes so treated, by separation of the lids to allow the purulent exudate to drain out, no evidence of panophthalmitis was observed, and by the end of

the fourth week healing was usually complete. But in animals exposed as above, with eyes untreated, lids allowed to remain sealed and exudate to accumulate, within three weeks there frequently developed a purulent panophthalmitis which by the sixth week usually destroyed the entire eyeball with complete suppuration of all orbital tissues. When a larger dosage was given, and the eyes untreated, a panophthalmitis might develop more rapidly. (Fig. 162.)

One series of four rabbits was treated with a heavy application of liquid dichlorethylsulphide to the center of the cornea. The amount applied was



FIG. 159.—Six weeks after direct application of standard droplet of dichlorethylsulphide to cornea. Combined ectropion and entropion of upper lid with resulting "ruffling" of lid margin. Ectropion of lower lid. Organization of the necrotic cornea with extensive arborizations of newly formed blood vessels, best seen in the upper half of the cornea. Even in the photographs these can be traced from the sclera across the superior arc of the limbus to the central portion of the cornea. The same eye is shown in Figures 160 and 161

about twice that of the standard application. In three rabbits the eyes were left untouched for five weeks, in the fourth for six weeks. After the first sealing of the lids there was no separation of them to allow the purulent exudate to escape. As a result an empyema of the conjunctival sac developed, with subsequent destruction of the eye from a suppurative panophthalmitis. These eyes all showed the same gross picture: Perforation of the cornea, necrosis and abscess formation, loss of the contents of the globe, and suppuration of all orbital contents.

In our cases the occurrence of panophthalmitis was due entirely to secondary infection, which occurred ultimately after several weeks in the untreated cases after slight gassing, but much more rapidly after heavier dosage. The pathologic changes produced by dichlorethylsulphide were covered up by those due to secondary infection.

FLUORESCEIN TEST

The standard method of applying an alkaline aqueous solution of fluorescein for the determination of corneal ulceration was carried out on a series of eyes at different time intervals following exposures to dichlorethylsulphide. A 2 per cent alkaline watery solution was used. Ten minutes after the direct application of the standard droplet to the center of the cornea several minute



FIG. 160.—Enlargement of Figure 159, to show details of changes

pin-point areas at the vertex of the cornea retained the fluorescent green coloration. These minute areas increased in number so that within 15 minutes after the exposure the vertex of the cornea appeared peppered with these spots in a small circular area. These pin-point areas increased in size and became confluent in about 30 minutes after exposure. By 1 hour they were fairly uniformly confluent. From this time on the fluorescein staining showed a gradually increasing depth of penetration and a spreading of the circumference of the staining area over the cornea, especially toward the inner canthus. The depth of the intravital staining reaction was greatest at the vertex of the cornea and decreased laterally. At the end of 48 hours a narrow crescentic area toward the outer canthus remained unstained, showing that the necrosis in this area occurred more slowly than elsewhere. After exposure to

the vapor of dichlorethylsulphide the fluorescein staining reactions were the same as after direct application. This intravital fluorescein staining was parallel in intensity to the necrosis of the corneal epithelium as shown by the microscopic study of the same stages. The earliest intravital staining occurred at the same time that the pycnosis of the corneal epithelium became evident, before any ulceration or abrasion took place. The use of this test was therefore of the greatest importance clinically in determining the severity and progress of the lesions and the effects of therapy.

SUMMARY OF GROSS PATHOLOGIC CHANGES

1. The standard drop of 0.0004 c. c. when applied directly to the cornea of animals was found to produce results practically identical with those produced by an exposure of 15 minutes to a vapor concentration of 1:20,000. The



FIG. 161.—Seven weeks after direct application of standard droplet of dichlorethylsulphide to cornea. Same eye as in Figure 159. Here given in profile to show marked irregularity of covered surface. Note especially the prominent apparent staphyloma in the sclera toward the inner canthus

criticism, therefore, that the use of the standard drop produces changes not comparable to those observed in exposure to dichlorethylsulphide vapor does not hold. Further, the use of the standard drop is a much more convenient and accurate way, as well as a safer method, of handling this material for experimental purposes. Moreover, the use of the direct-application method avoids the complication of respiratory or general cutaneous involvement following the exposure of the animal in a gas chamber.

2. Dichlorethylsulphide produces after one or two minutes exposure to drop or highly concentrated vapor a definite irritation of the conjunctiva with increase of lacrymation. Usually within 30 minutes there is a well-marked hyperemia, followed in an hour by the development of edema, which progresses rapidly up to the twelfth hour when there is usually a well-marked chemosis. Minute subconjunctival hemorrhages may develop as early as the tenth hour.

3. In animals the edema develops first and most markedly in the palpebral conjunctiva, following the direct application, while in the exposure to mustard-gas vapor it frequently develops first in the bulbar conjunctiva, this being practically the only difference observed in the effects of the two methods. By the end of the third day the edema begins to subside slightly, but persists to some degree for several weeks. In man the edema is less marked, more irregular, while the hyperemia is more marked, and minute vesicles may be found on the conjunctival surface.

4. The necrosis of the cornea is shown by a definite cloudiness developing in 5 to 6 hours, which usually at 8 hours has reached such a degree that the cornea takes on a porcelainlike appearance in the form of a very characteristic



FIG. 162.—Five weeks after direct application of dieblorethylsulphide to cornea. Dosage about twice the size of this standard droplet. Lids not separated. Eye untreated. Resulting panophthalmitis with collapse of eyeball

bluish-white opalescence. In the mildest cases the lesion does not progress beyond a slight cloudiness. Intravital staining with an alkaline aqueous solution of fluorescein shows very early the development of the corneal necrosis, even before ulceration has occurred. A striking phenomenon is the frequent occurrence of a more opaque band or line running horizontally across the cornea just below its transverse diameter.

5. A seropurulent exudate is well developed by the fifth to the sixth hour and increases until the eyelids are usually sealed by the accumulated exudate by the tenth hour. This adhesion of the lids remains a constant feature until the gradual subsidence of the inflammatory process about the third week. The edges of the lids remain sealed unless forcibly separated. If the eyes are fre-

quently examined with consequent separation of the lids and removal of the accumulated exudate, the stage of purulent exudation is perceptibly shortened.

6. With the subsidence of the edema a characteristic kinking or "ruffling" of the upper lid, a combined entropion and ectropion, appears, usually by the fifth or sixth day. At the same time the lower lid begins to exhibit a smooth ectropion.

7. Depilation of the lid hairs and of the face hairs, eventually about the entire orbit, takes place.

8. During the second week changes in the corneal curvature are constantly noted, some of these so marked as to appear staphylomalike.

9. Hypopyon sometimes occurs. Clouding of the contents of the anterior chamber occurs quite regularly in the later stages.

10. From the third week on the lesions slowly progress in a manner characteristic of the mustard-gas lesion of the skin toward resolution and repair. The "ruffling" of the upper lid increases up to the eighth week, while the ectropion of the lower lid frequently reaches the point of complete eversion. Progressive vascularization of the cornea takes place, the vessels usually reaching the center of the vortex by the end of the sixth week. Corneal cicatrization, marked impairment of vision, and thickening of the eyelids and nictitating membrane are the ultimate sequelæ. Even in the lighter cases in man, the edema and hyperemia of the conjunctivæ tend to run a chronic course with resulting disturbances and reduction of vision. An increased susceptibility to the vapor may develop. This susceptibility, however, is not a specific one.

11. Secondary infection. In animals exposed to the standard drop or vapor concentrations of 1:20,000, followed by treatment of the eyes, purulent panophthalmitis has not been observed to develop. In the case, however, of untreated eyes, and following heavier dosage, suppurative panophthalmitis does develop with complete destruction of the eyeball.

MICROSCOPIC PATHOLOGY

TECHNIQUE

Every care was taken to prevent the formation of artefacts, either post-mortem or technical. The eye was removed at once from the freshly killed animal by a wide incision encircling the lids and eviscerating the orbit. It was at once placed in the fixing fluids, a neutral formol being used for the greater part. The specimen was left in the fixing fluid about 48 hours before being sectioned, at which time uniform blocks of tissue were selected. These were so oriented as to give vertical sections through the entire eyeball, a section through the inner canthus and one through the lacrymal gland from each eye. The lens was removed from the eyeball after thorough hardening, in order to facilitate the cutting of thin sections. These tissues were embedded in paraffin. The sections were transferred to the celloidin sheet and stained with hemalum and eosin and by other ordinary staining methods.

PROTOCOL

RABBIT.—*One-quarter hour:* The changes observed were of slight degree, consisting of contraction and pycnosis of the corneal epithelium, which was more marked at the vertex and less marked over the limbus. Likewise the cells of the substantia propria showed a slightly greater degree of pycnosis and contraction than in control preparation. The bulbar and palpebral conjunctivæ showed a similar pycnosis and contraction. In the fornix there was

a more decided vacuolation of the conjunctival epithelium. The epithelium of the cutaneous surface of the eyelid showed also slight pycnosis and contraction. In the region of the inferior fornix alone did the subconjunctival connective tissue show a well-marked edema. In the upper fornix the edema was less marked. The lacrimal gland showed a marked distention of its gland spaces which were filled with secretion. Harder's gland and the tarsal glands showed no changes, likewise the sinus hairs. The blood vessels of all parts were anemic rather than congested. There was no hemorrhage and no thrombosis.

One-half hour: Changes identical with those above, except a little more marked in degree. Pycnosis and vacuolation were a little more pronounced. The edema was much greater, particularly around the lacrimal gland. The distention of the lacrimal gland was greater, and its cells showed a marked vacuolation. Greater congestion in all parts.

One hour: The only changes were an increase in the edema and congestion.

One and one-half hours: The pycnosis of the corneal epithelium was as above, but the substantia propria showed a distinctly more marked pycnosis of the corneal cells extending entirely through the cornea at the vertex. A large portion of the endothelium of the anterior chamber showed marked pycnosis and contraction. The conjunctival epithelium, both bulbar and palpebral, showed an increased degree of pycnosis, while the subconjunctival

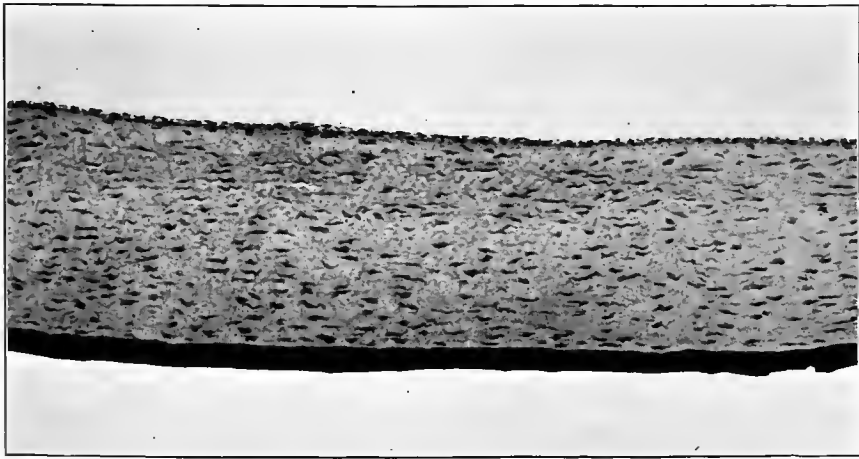


FIG. 163.—Cornea two hours after application of standard droplet of dichlorethylsulphide. First stage of necrosis of corneal epithelium and of the cells of the interstitial substance. Marked pycnosis of the corneal epithelium, the cells of the lowest layer alone being barely distinguishable. The nuclei of the interstitial substance and of the endothelial lining of the anterior chamber are also pycnotic. Section taken at corneal vertex

connective tissue showed a marked edema, extending entirely through the eyelids. It was especially noteworthy that many of the blood vessels appeared partly collapsed, with a relative anemia, while others were moderately congested. The lacrimal gland showed the same active secretion, many of the acini being greatly dilated, and filled with secretion. The vessels of the gland were congested and there was an increased number of wandering cells throughout the gland. The stroma of the gland and the surrounding tissues showed extreme edema. The tarsal glands showed groups of pycnotic alveoli. The epithelium of the membrana nictitans showed less change than that of the bulbar and palpebral conjunctivae.

Two hours: (Fig. 163.) Pycnosis of the corneal epithelium was complete. It was impossible to recognize the individual cells. The substantia propria stained more diffusely blue and the endothelium of the anterior chamber showed a greater degree of pycnosis and vacuolation. Similar changes occurred in the palpebral and bulbar conjunctivae and in the epidermis of the eyelids. The edema of the eyelids was now extreme, being most marked on the conjunctival surface. (See fig. 160.) There was an increase of wandering cells throughout both upper and lower eyelids, but no well-marked cellular infiltrations. Many of the blood vessels showed a well-marked congestion. The membrana nictitans showed a marked pycnosis of its epithelium and a marked edema of its stroma, its thickness being increased about tenfold. The lacrimal gland showed a marked distention of all its gland spaces and a marked vacuo-

lation of its epithelium which appeared distinctly more columnar in shape. The cells of Harder's gland stained very deeply and were contracted and pyknotic and had lost their granular appearance to a marked degree. The Meibomian glands showed a similar marked pyknotic involving all of the alveoli. The adipose tissue around the eye and about the tarsal glands showed a marked edema and gave a marked mucin staining reaction.

Three hours: The cornea was as before. The epithelium of the conjunctiva, both bulbar and palpebral, showed a greater degree of necrosis. The edema was much more marked beneath both the bulbar and palpebral conjunctiva, amounting almost to a liquefaction of the tissue. There was a well-marked polynuclear infiltration beneath the conjunctival epithelium extending throughout the entire lid. The epidermal surface of the eyelids showed now a well-marked pyknotic and erythema of the nuclei of the dermis, particularly of the papillary layer, with a well-marked polynuclear infiltration, the changes being identical with those described in the chapter on the skin lesions, with the exception that the cellular infiltration was somewhat more prominent than was found in the skin. The vessels showed a more marked congestion than in any of the previous stages. The lacrimal gland showed the same



FIG. 164.—Section of cornea at vertex five hours after direct application of standard droplet of dichlorethylsulphide. Desquamation of necrotic epithelium in center of vertex. Pyknotic of remaining epithelium and of cells of the interstitial substance. Complete necrosis of endothelial cells of anterior chamber

distention of the alveoli, but the cells were less columnar and the nuclei showed some pyknotic and erythema. The gland of Harder and the tarsal glands showed the same pyknotic as in the preceding stage. The changes in the epidermal surface of the eyelid had advanced in necrosis and cellular infiltration.

Four hours: Changes in the cornea appeared as in the preceding. Bulbar and palpebral conjunctivæ, membrana nictitans, and epidermal surface of eyelids showed increasing edema and cellular infiltration. The lacrimal gland showed extreme distention and the cells of many acini were flattened and vacuolated as in a state of exhaustion atrophy. Harder's gland presented a well-marked vacuolation of its epithelium, many of the cells showing large clear droplets, edema. Likewise the tarsal glands showed edema. In the palpebral and bulbar conjunctivæ the cellular infiltration was increased, and the lymph follicles in the palpebral conjunctiva contained great numbers of wandering cells. Vessels were greatly congested.

Five hours: (Fig. 164.) The corneal epithelium was in part desquamated over the region of the vertex, and about this the epithelium showed marked dissociation and vacuolation. The substantia propria stained lighter in color, many of its nuclei being only shadows.

At the sclerocorneal junction there was a well-marked infiltration of polynuclears, most marked just beneath the pycnotic epithelium. The upper and lower lids showed extreme edema (see fig. 160); and there was a marked infiltration of polynuclears throughout, which was more marked beneath the palpebral conjunctiva near the palpebral border. In this region the conjunctival epithelium was desquamating and an ulcerating surface was developing. The adherent dead epithelium was infiltrated with polynuclears. The blood vessels showed congestion. There was no thrombosis. On the epidermal border of the lids there was beginning desquamation of the dead epidermis. The sebaceous glands near the margin of the lid showed sebum retention. Likewise on the lower lid near the palpebral margin, there was noted the first development of ulcer or slough, and the membrana nictitans showed loss of its epithelium in areas. Lacrymal, Harder's, and tarsal glands, as in the preceding.

Six hours: Changes identical with above.

Eight hours: The only change noted from above was an increase in the extent of the ulcer on the conjunctival surface near the palpebral margin in both upper and lower lids, more marked in the upper. (Fig. 165.)



FIG. 165.—Section of palpebral conjunctiva eight hours after application of standard droplet of dichloroethylsulphide. Complete necrosis of epithelium. Marked congestion. Minute hemorrhages. Polynuclear infiltration

Ten hours: Cornea showed gradual loss of chromatin. Stained more palely. On the eyelids the necrosis of the epidermis and eschar formation had progressed while almost the entire conjunctival epithelium was completely disintegrated, forming a granular layer infiltrated with polynuclears. The exudate was most marked near the palpebral border where there was a distinct ulcer covered with exudate. Intense edema and congestion as in the preceding. Small pin-point hemorrhages occurred in the subconjunctival connective tissues.

Twelve hours: At the corneal vertex the cornea was dead throughout, having completely lost its nuclei. The corneal epithelium was desquamated over the vertex, and only here and there were faint outlines of the nuclei of the substantia propria. The pycnotic and vacuolated endothelium of the anterior chamber was still intact. The escharization of the epidermal surface of the lids was complete, and desquamation of both bulbar and palpebral conjunctival epithelium was nearly complete. Congestion was very marked and there were numerous minute hemorrhages by diapedesis both beneath the

epidermal surface and in the subconjunctival connective tissue. The edema was even more marked than in the preceding stages, involving the whole eyelid, and the lymphatics were enormously distended. The lacrimal gland was as before, but Harder's and the tarsal glands showed marked edema and liquefaction necrosis. There were masses of exudate, rich in polynuclears, adherent to the conjunctiva at the lid margins, the result of drying and concentration of the secretion, but near this, minute collections of polynuclears beneath the conjunctiva suggested beginning infection. The fluid of the edema at this stage assumed the same hyaline, finely granular, deeply pink staining appearance as was found in the subcutaneous tissues.

Fourteen hours: Changes as above, but slightly advanced. Intense congestion. Polynuclear infiltration of the muscle. Numerous hemorrhages about the greatly distended vessels. Secondary thrombosis beginning. More marked polynuclear infiltration into the subconjunctival connective tissue. Heavy granular precipitate in the distended alveoli of the lacrimal gland. These contained, likewise, great numbers of albuminous spherules, staining deep violet or pink, derived from the disintegration of the cells.

Fifteen hours: Changes as above with more marked polynuclear infiltration at the sclerocorneal junction, in the ocular muscle and in the orbital tissues. Beginning infection of the conjunctival ulcers near the palpebral border. Diffuse inflammation of the entire peribulbar tissues. It was a notable fact that the sebaceous glands on the epidermal surface of the lids showed penetration with the dichlorethylsulphide and necrosis, while the large ones at the palpebral margin seemed to escape.

Sixteen hours: Complete loss of the necrotic epithelium over the corneal vertex. Increasing polynuclear infiltration at the sclerocorneal junction. Edema of the ciliary body and ciliary ring. Increasing polynuclear infiltration and greater collection of pus at the palpebral borders.

Eighteen hours: Nearly complete necrosis of the cornea, except toward the periphery of the limbus. On the lids escharization was extending, the necrosis reaching into the subconjunctival tissue and into the subepidermal tissues on the cutaneous side. It was notable, however, that the subcutaneous necrosis was nearly through the depth of the lower border of the sebaceous glands. The epithelium of the entire margin of the lids was now completely necrosed and desquamated. Over the entire surface of the conjunctiva, including the membrana nictitans, the epithelium was necrotic and desquamating, but the necrosis extended but very little into the subepithelial connective tissues. For the first time changes were observed in the erectile sinus hairs of the upper lid, the epithelium of the hair follicle showing some pyenosis and contraction.

Twenty hours: Complete necrosis of the cornea, in the central portion extending to the endothelial lining of the anterior chamber which was partly necrotic and desquamating. Conjunctival, lid, and gland changes as above. The large sebaceous glands at the lid margin showed a more marked polynuclear infiltration than in any of the preceding. Congestion, edema, and minute hemorrhages as in preceding stages.

Twenty-two hours: Complete death of cornea in central portion, with loss of epithelium and endothelium of anterior chamber. Only scattered nuclei through the dead substantia propria. Eyelids showed the same extreme edema, congestion and numerous hemorrhages by diapedesis around the congested vessels as in the preceding, but with an increasing small-celled infiltration. Fibroblastic proliferation first observed in the subconjunctival connective tissue.

Twenty-four hours: Cornea completely necrotic except near the sclerocorneal junction. Its laminae were separated and there was a collection of fluid between the separated laminae. Edema at its height; other changes as above.

Twenty-six hours: Necrosis of the cornea complete with marked separation of the laminae into irregular spaces. Edema as in preceding, but polynuclear infiltration much more marked, extending throughout the entire thickness of the lids. Marked distention of the acini and atrophy of the cells of the lacrimal gland. Numerous capillary hemorrhages by diapedesis throughout the subconjunctival tissues, and the dermis of the lids. (Fig. 166.)

Twenty-eight hours: As in the preceding, no difference.

Thirty hours: (Fig. 167.) Identical with the preceding stages.

Thirty-two hours: Most marked changes in the cornea, particularly at the vertex. Surface roughened, knobby, laminae separated. Changes in lids and glands as in preceding.

Thirty-four hours: The central portion of the cornea showed complete necrosis but at the periphery there was a marked cellular infiltration and proliferation of corneal cells. At the sclerocorneal junction there was an evident fibroblastic proliferation. The edema of the upper palpebral conjunctiva was less marked; cellular infiltration about as before, but more cells of a fibroblastic type. The edema of the lower lid was the most marked yet seen, a large portion of the subconjunctival connective tissue showing complete liquefaction necrosis with marked polynuclear infiltration. (Figs. 168, 169.) The cutaneous border of the lower lid showed marked depilation. The lacrymal gland showed in various areas a very marked hypertrophy of the cells. These were more columnar, with a very deeply staining protoplasm. Other portions showed the light vacuolated cells as described above.

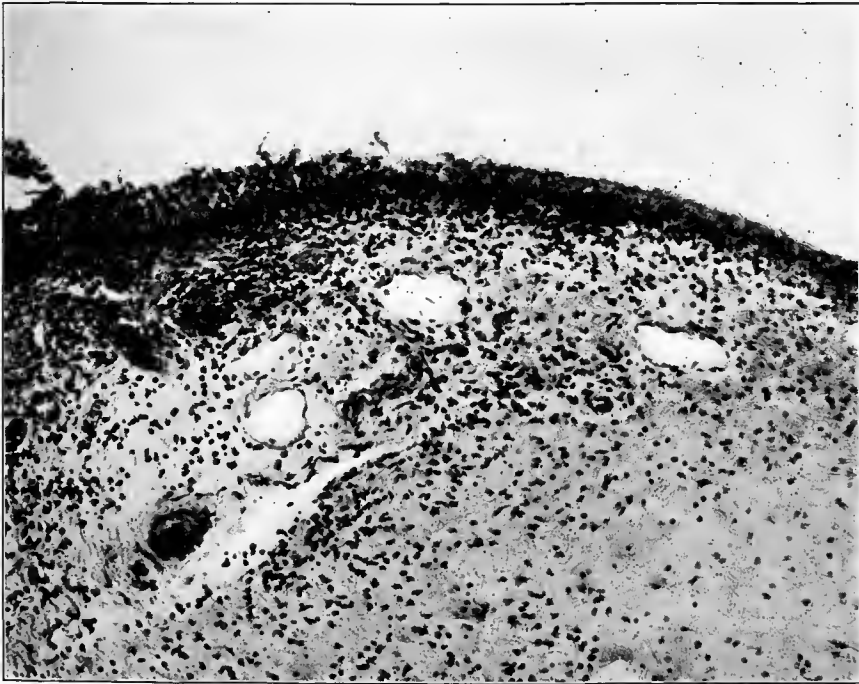


Fig. 166.—Palpebral conjunctiva 26 hours after application of standard droplet of dichlorethylsulphide, showing advancing necrosis, more marked infiltration, congestion, minute hemorrhages and edema

Thirty-six hours: Changes as in the preceding, except for the membrana nictitans which showed marked congestion of its vessels and multiple capillary hemorrhages. The ocular muscles showed marked edema.

Thirty-eight hours: The most marked necrosis of the cornea, the complete necrosis extending almost to the sclerocorneal junction. Complete necrosis of the endothelial lining of the anterior chamber with increased number of leucocytes in the fluid of the anterior chamber. On the lids there was beginning regeneration of the epidermis and hair follicles, but no evidences of regeneration of the conjunctiva. Almost complete depilation. Edema persistent in the subconjunctival tissues, and at the palpebral margins there was a marked collection of pus.

Forty hours: Necrosis of cornea less marked than in preceding individual; endothelial lining preserved. Appearances indicated a somewhat earlier stage, probably due to less intense action.

Forty-two hours: (Fig. 170.) Marked necrosis of the central portion of the cornea. The membrane of Descemet and the endothelium of the anterior chamber appeared as a hyaline red line bordering the anterior chamber. Proliferation of corneal cells at border of cornea;

fibroblastic proliferation at scleroconjunctival junction. Beginning separation of eschar on epidermal side of lids and also on the conjunctiva. Cutaneous lesion much deeper and more severe than the conjunctival, although the edema was much more marked on the conjunctival side, as was also the leucocytic infiltration.

Forty-four hours: Changes the same as at 42 hours, but of less intensity. Probably due to dilution of dose on the cornea. The skin surface of the lids showed marked escharization.

Forty-six hours: No essential differences.

Forty-eight hours: Corneal changes same as in the preceding. More marked escharization of the lids and conjunctival surfaces. Beginning separation of the eschar on epidermal portion of lids. Almost complete depilation.

Fifty hours: Very marked separation of corneal lamellae and formation of irregular spaces. Partial separation of the slough on the eustaneous surface of the eyelids. Well-marked regeneration of the hair follicles. Old hairs nearly entirely shed. The membrana nictitans was markedly hemorrhagic. The large sinus hairs showed marked necrosis of the epithelium of the hair follicle. Very marked fibroblastic proliferation in upper lid.

Fifty-four hours: Changes as in preceding, except for more marked escharization of the epidermal surface of lids, and more marked fibroblastic proliferation of the subcutaneous tissue. Marked congestion and numerous hemorrhages, particularly on the epidermal side of the lids.

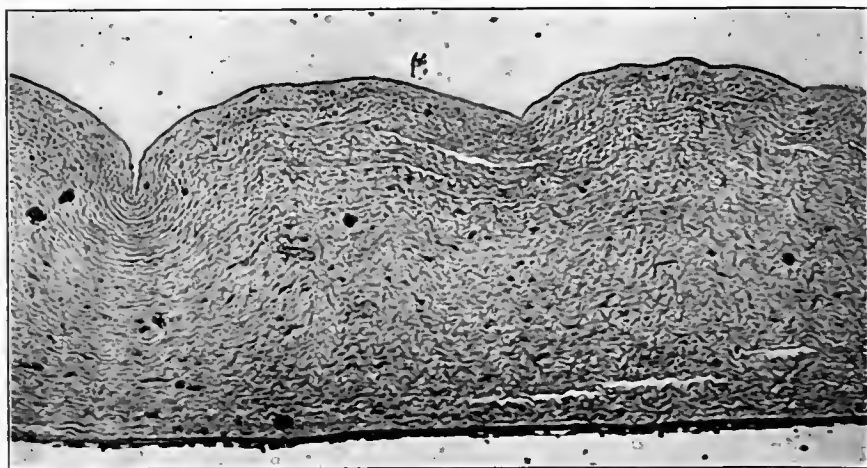


FIG. 167.—Cornea 30 hours after exposure to vapor of dichlorethylsulphide. Complete necrosis of cornea

Sixty hours: Shrinking and drying of the cornea at its vertex. Fibroblastic proliferation on the dermal side of the lids very marked. Epithelial regeneration well advanced. Beginning regeneration of conjunctival epithelium, but the greater part of the conjunctiva remained denuded. The lower lid showed many hemorrhages throughout its substance; the hemorrhages were more marked than in any other case. The eschar on the dermal side completely separated with the regeneration of the epidermis and hair follicles. Very few of the old hairs were left. Edema was still persistent on the conjunctival side, but less marked.

Sixty-five hours: Cornea showed regeneration of the corneal cells throughout its entire extent, but most marked at the periphery. There was marked regeneration of the endothelium of the anterior chamber with plasmodial masses of epithelium on the surface. Anterior chamber contained large numbers of leucocytes. Lids showed marked edema, extreme congestion, and multiple hemorrhages. Eschar on epidermal side was very deep and not completely separated. Changes much more severe than in the preceding instance with less regeneration and repair.

Seventy-two hours: Edema of lids still very marked. Deep escharization on epidermal side with eschar separating. Very little regeneration and repair. In the lower lid the edema was very marked, with liquefaction necrosis of the subconjunctival connective tissues.

Eighty-four hours: (Figs. 171, 172.) Complete necrosis of cornea, with no evidence of repair except at the limbus. Very marked congestion and numerous hemorrhages in the lids. Nearly complete depilation with regeneration of epidermis and hair follicles. Membrana nictitans markedly hemorrhagic and showed some fibroblastic proliferation.

Ninety-six hours: Cornea completely necrosed in the vertex. Proliferation of corneal cells toward the limbus. Fibroblastic proliferation near sclero-corneal junction. Very deep escharization of epidermal side of lids with separation of eschar. (Figs. 173, 174.) Regeneration of conjunctival epithelium in various portions of both upper and lower lids. Edema of lids much less marked, but lids were thickened by the marked fibroblastic proliferation.

One hundred ten hours: Cornea completely necrosed in central portion. At limbus it showed polynuclear infiltration and fibroblastic proliferation. Anterior chamber contained numerous polynuclears, pus. Iris and ciliary body showed cellular infiltration. Conjunctiva showed areas of regeneration of epithelium. Edema was less marked. The gland of Harder showed liquefaction necrosis, as did also the tarsal glands. Necrosis of the epidermal side was deep, but the eschar had nearly completely separated and there was regeneration of the epithelium in some areas and of the hair follicles. Edema of lids was much less marked but the lids were thickened by the connective-tissue proliferation. The membrana nictitans showed almost complete regeneration of its epithelium.

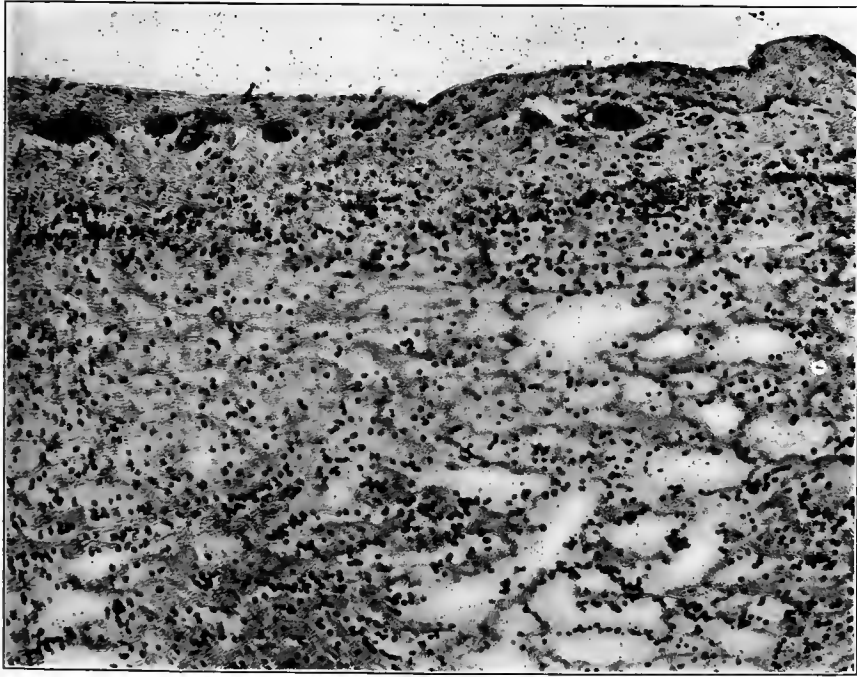


FIG. 168.—Palpebral conjunctiva 34 hours after application of standard droplet of diethylethylsulphide. Section at fornix of upper lid showing the complete loss of the necrotic surface, extreme edema, and polynuclear infiltration

Five days: There was some regeneration of the corneal epithelium and proliferation of corneal cells and infiltration of leucocytes throughout the entire cornea. The edema of the bulbar conjunctiva was still very marked while that of the palpebral was very much less. The subconjunctival lymph follicles were very hyperplastic. Large dilated lymphatics showed, however, in the subconjunctival connective tissue of the lids. The escharization of the epidermal side was very deep, extending below the hair follicles, and there was no repair. In the lower lid the edema fluid showed marked fibrin formation.

Six days: Regeneration of the corneal epithelium over the limbus and extending in a delicate layer over the vertex. Endothelium of anterior chamber was regenerating. Marked regeneration of the epithelium of the palpebral conjunctiva with overformation of epithelium. Regeneration less marked on the epidermal surface. Lymph follicles hyperplastic. The bulbar conjunctiva still showed marked edema without much cellular infiltration

Seven days: (Fig. 175.) Marked regeneration of the cornea with great thickening, the cornea being more than twice as thick as normal, but the thickness varied in different portions. Marked infiltration of leucocytes and marked proliferation of the cells of the substantia propria. Around the periphery there was a marked formation of new blood vessels extending into the limbus and reaching nearly to the vertex. Marked regeneration of the endothelium of the anterior chamber. Sections cut in some planes of the cornea showed a failure of regeneration of the corneal epithelium and a very marked infiltration of the anterior lamellæ. The conjunctival epithelium showed marked regeneration while the eschar of the epidermal portion of the lids had not yet separated. The bulbar conjunctiva still showed marked edema of the subconjunctival tissue. The lids were thickened by the marked fibroblastic proliferation. There was intense congestion and many capillary hemorrhages.

Eleven and one-half days: Cornea thickened irregularly from leucocyte infiltration and proliferation of cells of the substantia propria. At the periphery the escharization was quite marked extending onto the bulbar conjunctiva, beneath which there was a marked leucocyte



FIG. 169.—Section from the same region as in Figure 168, but taken deeper down, showing the extreme edema and liquefaction necrosis, below the narrow band of the sphincter orbicularis

infiltration. The conjunctiva showed marked regeneration of its epithelium, infiltration of the subepithelial tissue and hyperplasia of the lymph nodes. On the epidermal surface there was a very marked eschar formation which was partly adherent and partly separated. Beneath it there was advanced regeneration of the surface epithelium and of the hair follicles. The membrana nictitans was much thickened, its epithelium nearly regenerated, and it showed a marked proliferation of new blood vessels with very hypertrophic endothelium.

Twelve and one-half days: Changes identical with the preceding. The hyperplasia of the subconjunctival lymph nodes was very marked.

Two weeks: Cornea very irregular in thickness. Showed less evidence of regeneration and repair than the preceding. New blood vessels extending into it from the periphery. Eyelids showed marked regeneration of epithelium both on the conjunctival and on the skin side. Large nests of cells proceeding from the hair follicles.

Three weeks: Regeneration of corneal epithelium and endothelium of anterior chamber. Marked proliferation of blood vessels around the periphery of cornea and formation of scar tissue replacing the corneal substantia propria. Great irregularity in thickness of cornea. Eyelids showed advanced repair and regeneration of the epidermal surfaces and of the con-

junctival surface. Edema still present on the conjunctival side. The regenerating hair follicles and sebaceous glands formed large atypical cell nests. The sinus hairs showed fibroblastic obliteration of the cavernous spaces and atypical proliferations of squamous epithelium suggesting newly formed sebaceous glands.

Four weeks: (Figs. 176, 177, 178.) The cornea showed throughout regeneration of its epithelium and of the endothelium of the anterior chamber. It was very irregularly thick-

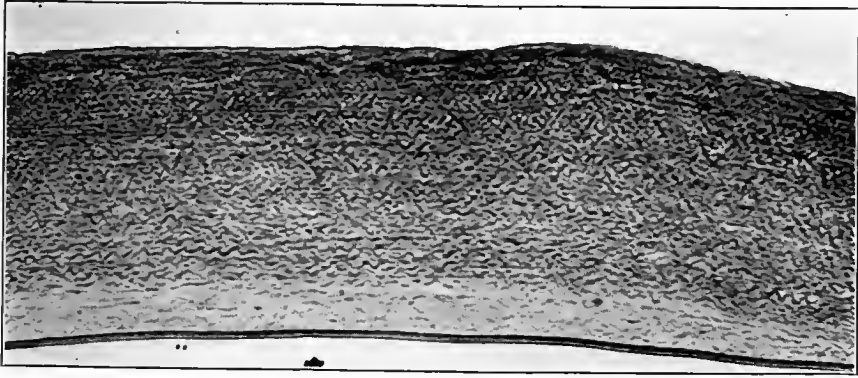


Fig. 170.—Cornea 42 hours after application of standard droplet of dichlorethylsulphide. Membrane of Des-cemet appears as a bright hyaline line staining red with eosin

ened and had an uneven surface. From the periphery great numbers of newly formed vessels extended up toward the corneal vertex, on one side reaching halfway across the cornea. These vessels were much more numerous on the anterior side of the cornea, and many of them were very large and dilated. On one side near the scleral junction there was a large area of subepithelial edema infiltrated with leucocytes, producing an elevation on the cornea, as described in the gross notes. Other sections of the cornea showed it to be heavily



Fig. 171.—Cornea 3½ days after application of standard droplet of dichlorethylsulphide. Complete necrosis of corneal tissue; ulceration of surface; beginning infiltration with polynuclear leucocytes and collection of polynuclear leucocytes along the line of the necrotic endothelium

infiltrated with pus cells between the newly formed blood vessels. Regeneration of conjunctival epithelium was complete, except near the palpebral margin, where there was an ulcer. Edema of the subconjunctival tissues was much less marked than in the preceding. Harder's and the tarsal glands showed marked lymphoid infiltration. Lacrymal gland more normal in appearance. Hair follicles showed new formation of hairs. The large sebaceous glands at the palpebral margin were hyperplastic, and the lymph nodes of the conjunctiva were also hyperplastic.

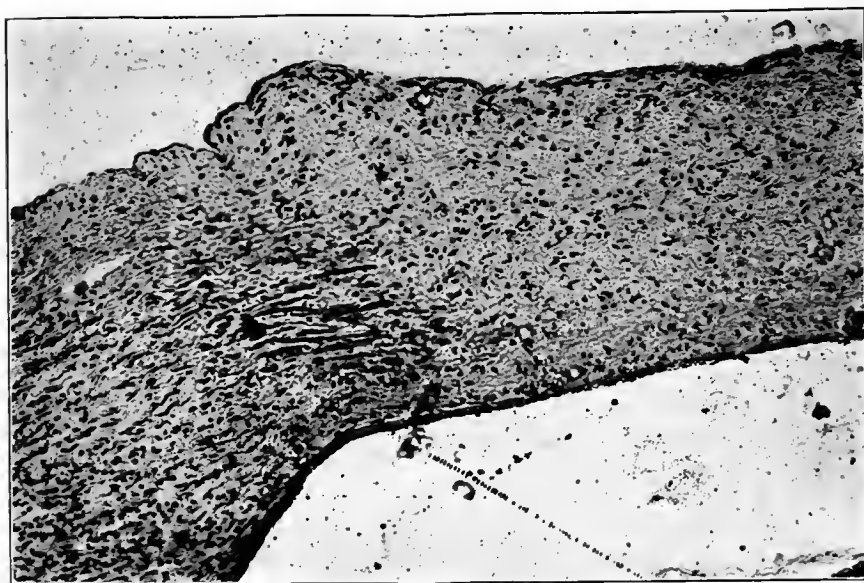


FIG. 172.—Section of scleroconjunctival junction 3½ days after application of standard droplet of dichlorethylsulphide. Infiltration of leucocytes beginning fibroblastic and angioblastic proliferation

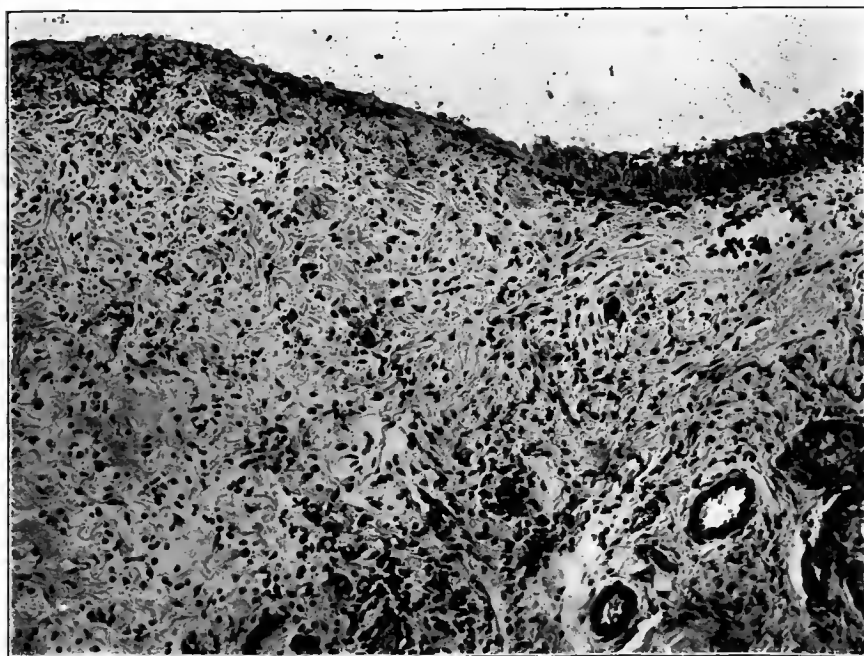


FIG. 173.—Section of upper lid at palpebra margin four days after direct application of standard droplet of dichlorethylsulphide. Advanced ulceration beginning repair

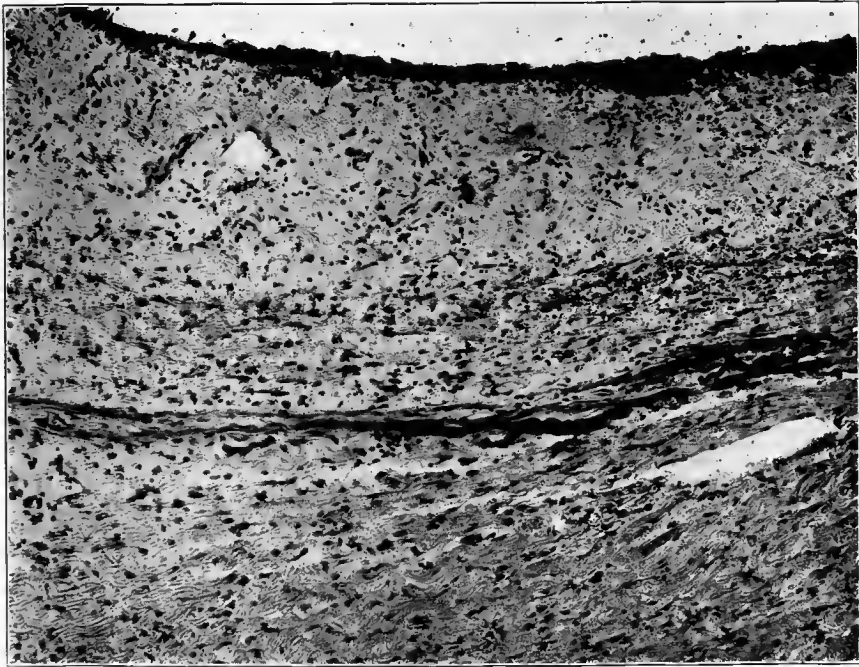


FIG. 174.—Section of same lid near fornix. Regeneration of the conjunctival epithelium. Disappearance of the edema and advancing cicatrization of the subconjunctival tissues



FIG. 175.—Section of corneal vertex seven days after application of standard droplet of dichlorethylsulphide. Ulcerated surface. Infiltration of necrotic cornea with polynuclears and scattered fibroblasts. Beginning regeneration of endothelium

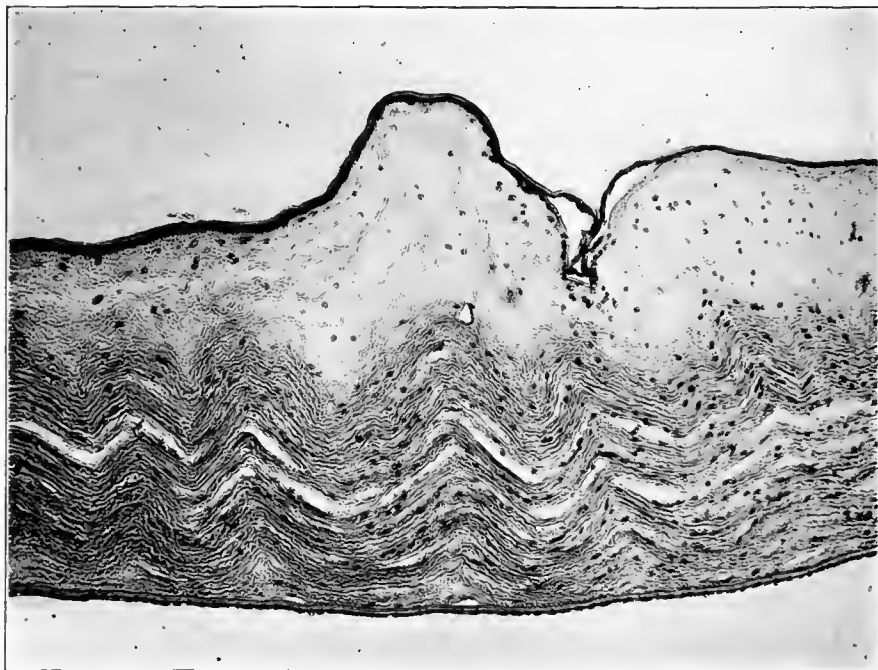


FIG. 176.—Section of corneal vertex four weeks after application of standard droplet of dichlorethylsulphide, showing the marked irregularities in the corneal surface; regeneration of corneal epithelium and endothelium of anterior chamber; edema of the interstitial substance with some fibroblastic repair

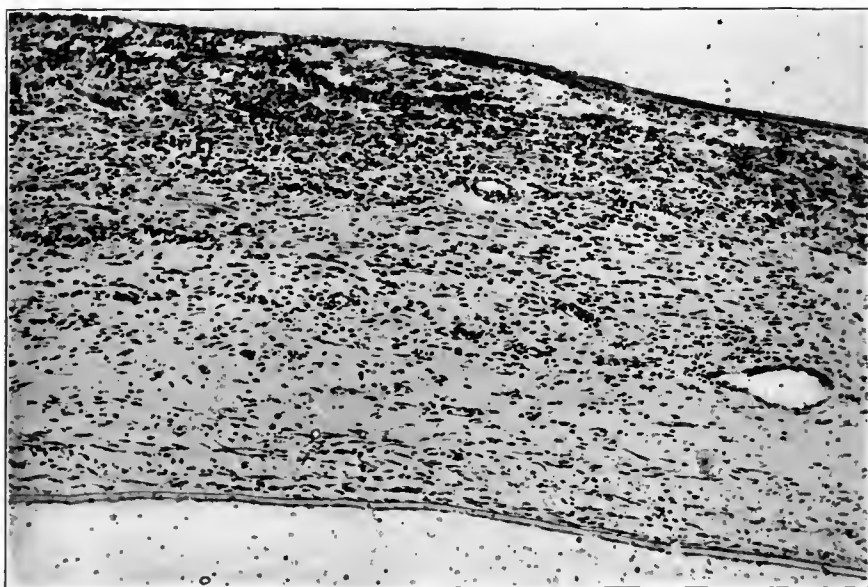


FIG. 177.—Sclerocorneal junction of same eye as in Figure 176, four weeks after application of standard droplet, showing vascularization and repair proceeding from the sclera

Seven weeks: (Figs. 179, 180, 181, 182.) The cornea was markedly but very irregularly thickened throughout, heavily infiltrated with leucocytes, and showed throughout its extent a marked new formation of blood vessels. Substantia propria was largely replaced by fibrous connective tissue. The membrane of Descemet showed as a clear hyaline line and the endothelium of the anterior chamber was regenerated in a flat layer over this. The regeneration of the epidermal surface of the lids was complete. The sebaceous glands were approaching normal size. The edema has almost entirely disappeared except over the bulbar conjunctiva. Lacrymal gland still hypertrophic. Lymphoid tissue in Harder's gland was hyperplastic, as were also the subconjunctival lymph nodes. The lids and nictitating membrane were thickened from the new formation of connective tissue.

Dog.—A small series was also carried out upon dogs. The changes were essentially the same in kind, although apparently of greater intensity. A marked hemorrhagic condition of the conjunctiva was noted in the earlier stages.

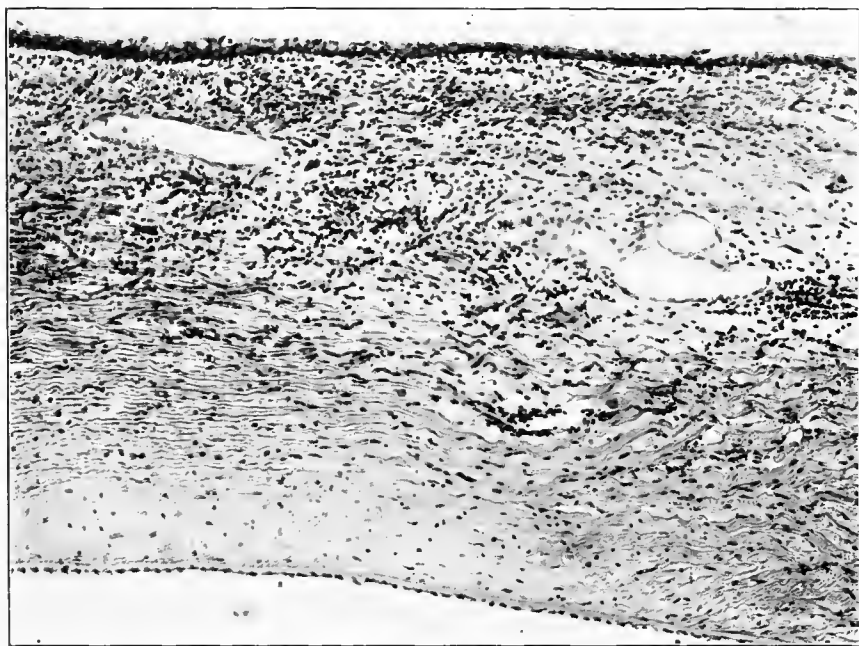


FIG. 178.—Section of corneal limbus 4 weeks after application of standard droplet of dichlorethylsulphide. Advancing repair into the cornea from the scleroconjunctal junction

EXPOSURE TO DICHLORETHYLSULPHIDE VAPOR

Rabbit.—Series of animals exposed for varying periods to varying concentrations of mustard-gas vapor (1:20,000 to 1:50,000) and killed at intervals of 12 hours to 4 days after exposure in the gassing chamber showed changes of precisely the same kind as the animals treated with the standard droplet of the liquid. It was found that a 15-minute exposure to a 1:20,000 concentration produced changes identical in degree with those produced by the standardized drop of liquid. It is noteworthy in these experiments with the weaker concentrations of the gas that the cornea first showed evidences of necrosis and then the skin surface of the lids, while the conjunctival epithelium did not undergo necrosis, and the conjunctiva itself presented only the picture of a mild conjunctivitis with an unusual degree of edema, particularly of the bulbar conjunctiva in the earlier stages, and of the palpebral in the later.

The epidermal changes were in all cases much more severe than the conjunctival, marked necrosis of the former occurring when no necrosis of the conjunctival epithelium was observed. The corneal necrosis was always most severe at the corneal vertex. In all cases exposed to the gas the lesions were most intense in the portion of the conjunctiva and cornea exposed in the palpebral fissure, and the lesions therefore were much less diffuse than when direct application was used, thus resembling more nearly the human cases.

DIRECT APPLICATION OF MUSTARD GAS LIQUID TO THE EYES OF DEAD ANIMALS, THE EYES SO TREATED BEING EXAMINED AT INTERVALS

Microscopic examination of eyes to which dichlorethylsulphide had been applied post-mortem showed no changes attributable to the action of the mustard-gas liquid.

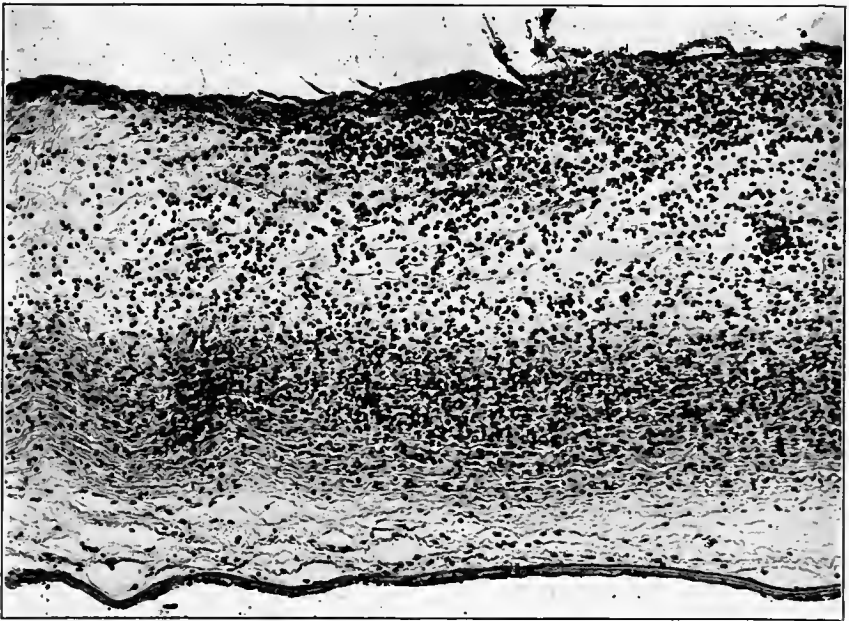


FIG. 179.—Section from the inferior portion of the cornea seven weeks after application of the standard droplet of dichlorethylsulphide. Persistent ulcer; marked polynuclear infiltration of the cornea, and repair. Blood vessels have reached the center of the cornea

SUBCUTANEOUS AND INTRAVENOUS INJECTIONS OF DICHLORETHYL-SULPHIDE

Animals so treated died within five hours after the intravenous injection of 1 minim and uniformly in four to five days after the subcutaneous injection of 1 minim. Microscopic examination of the eyes of these animals showed no evidence of conjunctivitis or other lesions.

EYES SHOWING SECONDARY INFECTION

Four cases showing panophthalmitis, three at five weeks and one at six weeks, showed microscopically a diffuse suppurative process involving all the structures of the eye and of the orbit. The suppurative process began first in the cornea, and in the earlier stages might show as small pin-point abscesses

in the substantia propria, each surrounding a colony of cocci. The process extended through the anterior chamber toward the posterior portion of the eyeball until ultimately all was involved. Similar changes were observed in a dog three weeks after exposure, the earlier infection in this case resulting from the lack of care and the lessened resistance of this especial animal.

CHANGES IN ORBITAL TISSUES

In the uninfected cases the changes consisted of congestion and edema, and a mild diffuse inflammation involving particularly the ocular muscles. In the infected cases there was a diffuse suppurative process.



FIG. 180.—Section from inferior portion of corneal limbus, seven weeks after application of standard droplet of dichlorethylsulphide. Partial regeneration of corneal epithelium. Marked polynuclear infiltration and advanced vascularization and repair of the substantia propria. Regeneration of the endothelium of the anterior chamber

SUMMARY OF THE MICROSCOPIC PATHOLOGY

1. The microscopic changes produced by the direct application of the standard droplet of the liquid and by exposure for 15 minutes to a vapor concentration of 1:20,000 were identical.

2. *Changes in the cornea.*—The earliest changes noted were in the cornea, consisting of pycnosis and contraction of the epithelium and of the substantia propria, most marked at the corneal vertex and extending to Descemet's membrane. This was followed by a loss of nuclei until by the twelfth hour the corneal vertex showed complete necrosis, the necrosis often extending through the limbus nearly to the scleral junction. Desquamation of the dead corneal epithelium began in about 5 hours. Polynuclear infiltration of the sclerocorneal junction began in 5 to 6 hours. Fibroblastic proliferation was first noted at 34

hours at the sclerocorneal junction. Earliest signs of regeneration of the corneal substantia propria were noted at the periphery at 65 hours. New formation of blood vessels into the limbus was well marked as early as 7 days. Slow repair of cornea continued for several weeks, with development of a highly vascularized corneal cicatrix. Marked changes in the corneal thickness occurred as the result of separation of the lamellæ, edema, cellular infiltration, and fibroblastic proliferation. The severity of the corneal lesion was in direct proportion to the concentration of the gas and the period of exposure.

3. *Changes in the conjunctiva.*—Necrosis and desquamation of a large part of the conjunctival epithelium resulted, but it is noteworthy that this necrosis was much less in degree than that of the cornea or of the skin surfaces

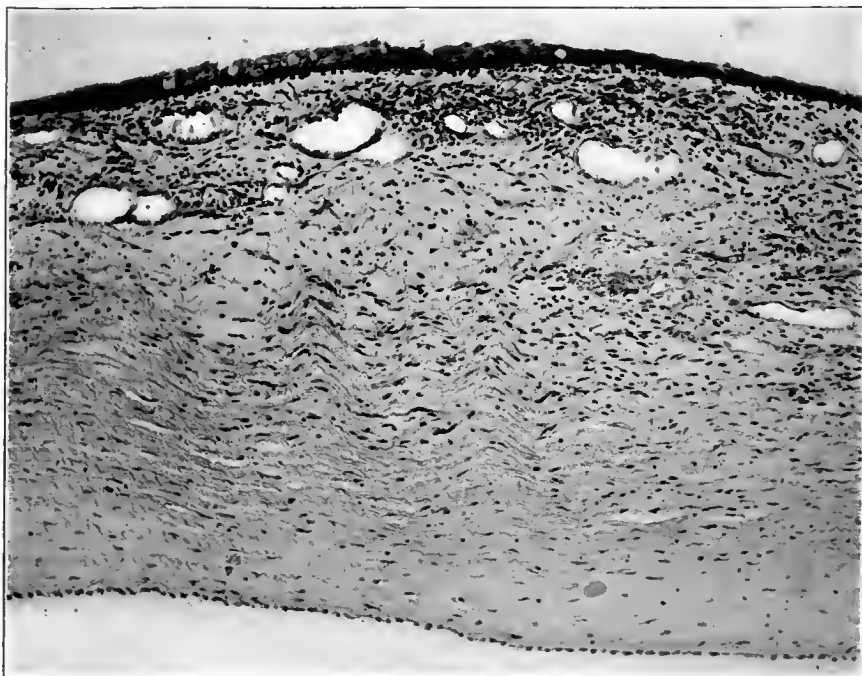


FIG. 181.—Section from the superior half of the corneal vertex seven weeks after application of standard droplet of dichlorethylsulphide, showing the greater degree of cicatrization usually found in this portion

of the eyelids. The primary necrosis rarely extended beneath the basement membrane of the palpebral and bulbar conjunctiva, except at the palpebral margin, where collections of a serofibrinopurulent exudate occurred. Here shallow ulcers were produced. The most striking feature of the conjunctival involvement was the extreme edema of the subconjunctival connective tissues, which was usually most marked in the bulbar conjunctiva near the scleral sulcus and in the palpebral conjunctiva of the upper lid. This was so extreme that liquefaction necrosis in this tissue, with marked leucocyte infiltration, usually followed. Petechial hemorrhages were of frequent occurrence in the subconjunctival connective tissue. Regeneration of the conjunctival epithelium occurred readily and healing took place with a permanent thickening of the conjunctiva due to the formation of fibroblastic tissue.

4. *Structures of eyeball*.—(Figs. 183, 184.) Iritis and iridocyclitis, with exudation into the anterior chamber, occurred without infection in the severest forms of gassing, and were common occurrences at about the third to sixth week in the uncared-for cases as the result of secondary infection even when the gassing was light. In the cared-for cases of average exposure, no changes were observed in iris, ciliary body, chorioid, retina and optic nerve, except congestion and edema.

5. *Nictitating membrane*.—Changes observed in rabbits were necrosis of the epithelium, extreme edema, multiple hemorrhages, congestion, and eventually more or less marked thickening from connective-tissue proliferation.

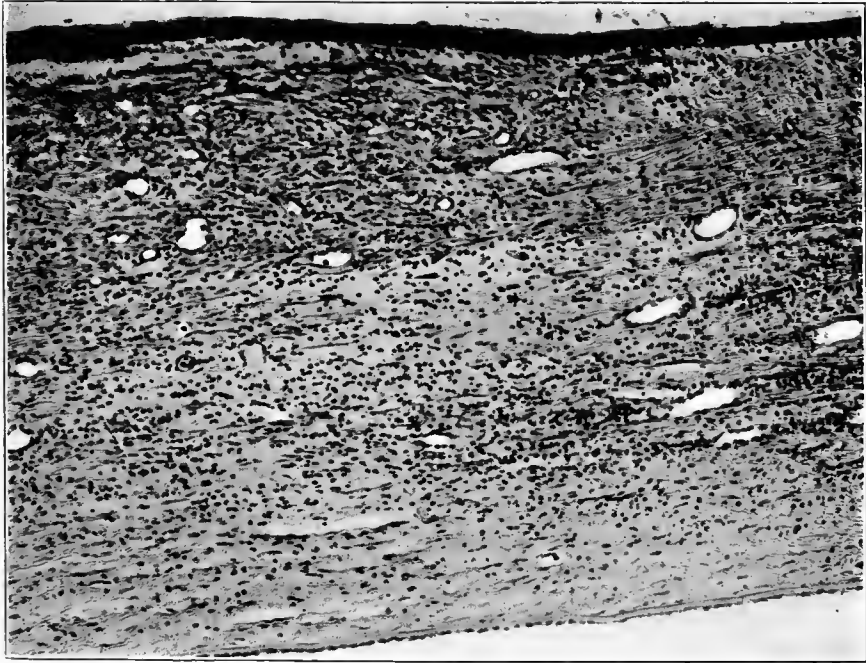


FIG. 182.—Section of corneal limbus from same eye as Figure 181, showing advanced cicatrization

6. *Lacrimal gland*.—Increased functional activity was noted at all times; ultimately, overuse atrophy and subsequent hypertrophy. Increased albumin content was observed in the secretion.

7. *Harder's gland*.—Parenchymatous degeneration and inflammatory infiltration occurred.

8. *Tarsal glands*.—Evidences of penetration into the tarsal glands were shown by degeneration and necrosis of certain of the acini. Leucocyte infiltration occurred about and into these glands.

9. *Skin surface of eyelids*.—The same changes were observed in the cutaneous surface of the eyelids as were described in the chapter on cutaneous lesions. The important influence of the sebaceous glands and hair follicles in permitting the entrance of the gas into the deeper tissues of the dermis was strikingly shown here, the penetration into and resulting escharization of the skin being greater than in the case of the cornea or the conjunctiva.

10. *Subconjunctival tissues*.—The relatively slight penetration into the subconjunctival tissues might be explained as the result of the protection afforded by the moistness of the surface and lacrymation.

11. *Orbital tissues*.—In the cared-for cases congestion, edema, and a mild diffuse cellular infiltration, particularly in the orbital muscles, were noted; in infected cases a diffuse suppurative cellulitis occurred.

CLINICAL CASES ^d

CASE 1 (fig. 185).—Exposed to strong concentration of mustard-gas vapor for 10 to 12 minutes. Patient wore a gas mask. The eyes began to burn and be painful, lacrymated freely, and were red and inflamed two hours after exposure. Three to four hours after exposure he began to feel as though there were granules beneath the eyelid. He could not

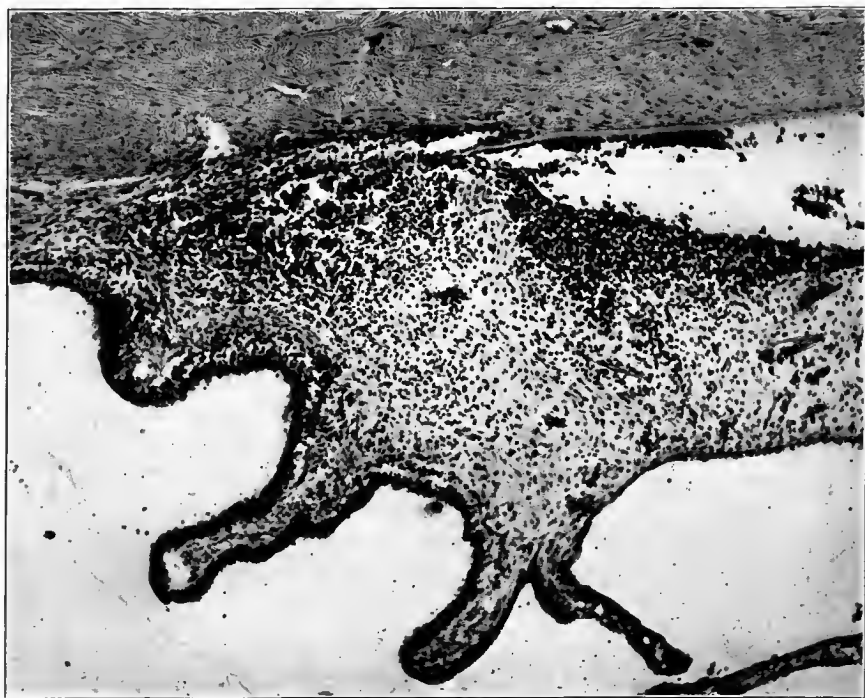


FIG. 183.—Ciliary body from eye of rabbit exposed 12 hours in gassing chamber to a concentration of 1:50,000. Animal died 92 hours later. Marked collection of polynuclear leucocytes in anterior chamber, in the ciliary body, and in the iris of the left eye, which had received no treatment with the dichloramine-T solution

keep his eyes closed because there was much more pain when the lid borders were approximated. He was very sleepy, because of much loss of rest due to night work, and his eyelids felt heavy. He went to bed. Boric acid compresses (cold) were applied. American oil was instilled once; it did no good. The compresses were to be continuous; they relieved the pain, but he could bear them only about one-half hour at a time through the night. For 3 to 4 days argyrol was instilled once in 24 hours, and did very little good. The palpebral conjunctiva appeared "blistered" the morning after the exposure. The irritation continued for 3 to 4 days, but gradually decreased in severity. The congestion decreased but was still marked. In fact it was present and quite distinct 31 days after exposure. The patient complained of "misty" blurring of vision, which was marked at first and then decreased, but was still present three weeks after exposure. The bright sunlight hurt his eyes, the lids felt heavy. There was no interference with accommodation so far as the patient knew. He was able to read about the tenth day, but could read only a page at a time.

^d For the opportunity of examining the clinical cases, and for their histories, we are indebted to Capt. L. L. Roos, M. C.

Examination.—Congested dilated vessels on the bulbar conjunctiva from the border of cornea, over the limbus, to the inner and outer canthus in each eye. The congestion and thickening of the bulbar conjunctiva showed in the palpebral aperture. The palpebral conjunctiva, especially superiorly, showed slight thickening.

CASE 2 (fig. 186).—Exposed 10 to 12 minutes to a strong concentration of mustard gas vapor. He wore a gas mask at the time. Sulphur dichloride and sulphur monochloride had always irritated his eyes. He first noted irritation under the arms about four hours after exposure, and just one hour later—that is, five hours after exposure—there was a stinging irritation “just like salt” in the eyes. One drop of “Silvol” solution was put in each eye. This increased the pain. The eyes lacrymated profusely and the eyeballs were red and the vessels congested. Boric-acid compresses (cold) were applied at intervals all night. At 3 a. m. he found that he could open his eyes only to a slight extent, the aperture was only about one-half inch at the greatest. The lids were edematous, and this prevented the opening of the eyes. The morning after the exposure the eyes were completely closed

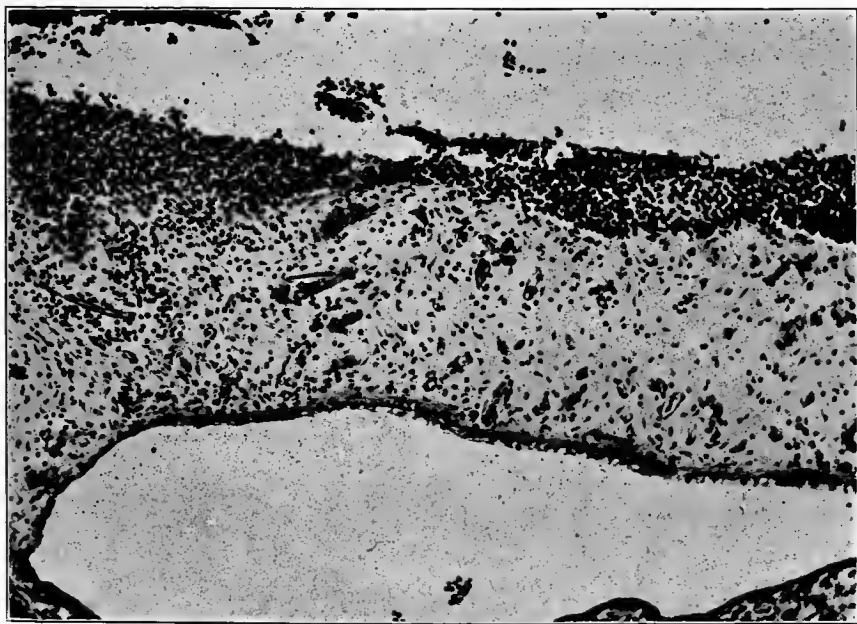


FIG. 184.—Iris of same eye as in Figure 183, showing congestion, edema, and polynuclear infiltration. Marked polynuclear exudate in the anterior chamber

and the lashes were “glued together” by the thick purulent exudate. He could not open the eyes wide enough to see anything. At the first-aid room argyrol and sterile American oil were put into the eyes, and he was put to bed and cold or iced boric compresses were put on continuously for 5 days. Argyrol was instilled $3\frac{1}{2}$ days after exposure for about 30 minutes and everything both near and far was found to be blurred. The conjunctiva was congested. For more than 10 days the eyes lacrymated profusely, especially the left eye. On the fifth day his vision was clearer but very much impaired. He could not distinguish letters at all on a printed page. He could not read ordinary print for 10 days, and then he could read the print for only 10 minutes at a time until the eyes ached and things became blurred. It was not until the eighteenth day that he could read for an hour at a time. His vision for distance gradually improved, but was still somewhat blurred. After 18 days, at the end of the third week, near vision was such that he could not read much more than $1\frac{1}{2}$ hours at a time and then he must rest 2 to 3 hours.

Examination.—Thickening of the conjunctiva in the palpebral fissure was especially marked in the triangle with apex at the inner canthus and base at the inner limbus. The thickened conjunctiva was yellowish. The vessels were slightly congested. The palpebral conjunctiva was not very much changed, possibly slightly thickened.

CASE 3.—Pvt. Mc. Exposure of 40 minutes in four shifts to strong concentration of mustard gas vapor while wearing a gas mask. The eyes had been congested for two days because of exposure to hydrochloric-acid gas. On entering the infirmary at 6 p. m. he had no eye symptoms, but because of the congestion the eyes were irrigated with sodium bicarbonate solution or boric acid. He was very nauseated and sick, and vomited and retched very much. At the same time he complained of severe sharp pains in the eyes. Boric-acid compresses were applied continuously for three days, and the eyes were washed with the boric acid about every 15 minutes for the entire first night. The eyes were very painful burned, and felt as though an electric current was passing across and through the anterior



FIG. 185.—Congestion of the conjunctival vessels persisting to a marked degree, four weeks after exposure to dichlorethylsulphide vapor

part of the eye. The eyes were swollen and a purulent exudate glued the eyelashes down. On the third day, while his eyes were being opened and argyrol instilled, he had a flash of vision for a second, just long enough to see his nurse. On the fourth day he recognized individuals. He had been able to open his eyes about the fourth night, but he could see only a dull light. On the fifth day he opened his eyes slightly and everything was blurred; near and distant vision were equally impaired. He was not able to read for about 14 days, and then only for about 5 minutes at a time, gradually becoming able to read more and more, but at 6 weeks he could read only about 1 to 2 hours at a time. When in the sunlight, however, there was a feeling of "wideness" (of the palpebral opening), some blur, and some discomfort, and slight photophobia.

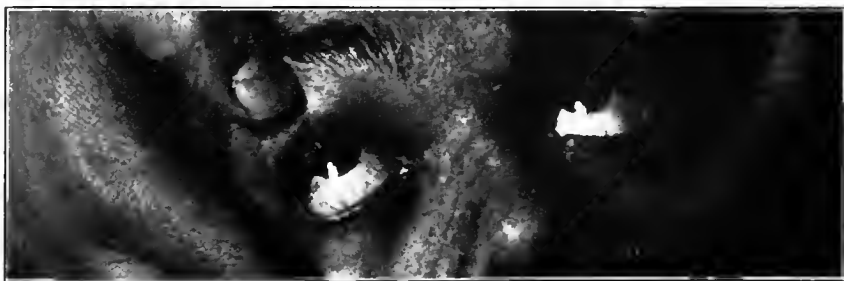


FIG. 186.—Persistent congestion four weeks after exposure to dichlorethylsulphide vapor. Acute symptoms were very severe and the patient still complained of dimness of vision when he left the hospital after five weeks

Examination.—In the morning there was slight purulent exudation, which glued the eyelashes together; there was a small drop of purulent exudate in the inner canthus. There was a slight blepharitis marginalis. The ocular conjunctivae showed thickened, slightly yellowish, elevated areas, pingueculae, on either side of the corneae. The vessels were large, slightly dilated and congested. The palpebral conjunctiva showed nothing of any great interest.

CASE 4 (fig. 187).—Exposure of 30 minutes to strong concentration of the vapor of dichlorethylsulphide while wearing the gas mask. He was first exposed at about 3.30 p. m. and noticed his first symptoms at about 5 p. m. These were irritation, burning, and lachrymation of the eyes and a "faint feeling" in the pit of the stomach. Then on leaving the

infirmary and getting into "the air" the eyes felt better and he was not troubled until he returned to the infirmary. Here, after taking the routine "shower, kerosene rub, and shower" treatment and retiring, his eyes felt very painful, with the sensation of fine sand under the lids, and there was profuse lachrymation. A thick serous exudate made the eyelashes mat together and seal the eye. His vision was blurred, probably due to the increased lachrymatory secretion. The eyes were red and congested, according to his roommate. His eyes were irrigated with boric acid; American oil was instilled, and cold boric-acid compresses were applied continuously for five days. Argyrol was used from the second day until about the fifth day. The eyes could not be opened, because the lids were swollen, edematous, and glued together at the margins by the matted lashes. After the third day he was able to hold the eyes open for a few minutes at long intervals, but it was not until the fifth day that he could dispense with the compresses. His vision had been very blurred, but cleared fairly well on the fifth day. There was some yellowish exudation with considerable serous exudation. The eyes were washed frequently during the day with boric-acid solution. A hordeolum formed on the upper eyelid, near the inner canthus, on about the fourteenth day. The patient did not attempt to read for two weeks, and when he did begin he noticed no trouble, except that the eyes ached after he had read a quarter to half an hour. He could not read magazines until about ten days later.

Examination.—The bulbar conjunctiva showed the same features as in the other cases, but to a more marked degree; there was a thickening and a yellowish color, with marked congestion of the vessels of the part of the conjunctiva that was exposed in the palpebral

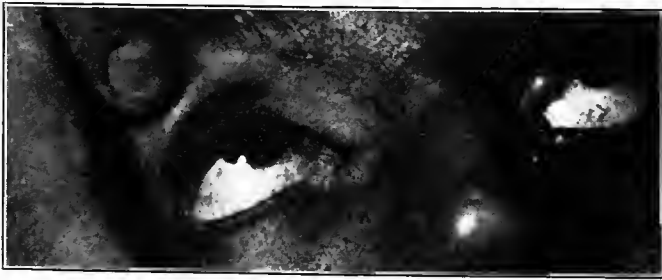


FIG. 187.—Marked conjunctival congestion and hordeolum of left upper lid in a case of severe mustard-gas conjunctivitis, four weeks after exposure. The hordeolum is a part of the general staphylococcus furunculosis which may characterize the later stages of the severe skin burns

fissures on either side of the cornea. At the limbic border a number of straight, small, deep vessels were seen to be injected and suggested a deeper penetration and a sclerociliary injection. The conjunctiva from the inner limbus to the inner canthus was more markedly involved.

CASE 5 (fig. 188).—Exposed 30 to 45 minutes in several shifts to strong concentration of dichlorethylsulphide vapor while wearing gas mask. Began on the evening shift at 4 p. m. and first exposed himself at this time. He noticed no eye symptoms until about 10 p. m., when there was burning, a feeling as though granules were under the lids, and a fairly profuse lachrymation. Cold boric-acid compresses and boric-acid eye washes were employed during the night and for several days. The routine treatment, as given, together with argyrol instillations, was employed. According to the physician in charge, the patient was in severe shock. There was some pain, blurred vision for near and distant objects, and a profuse lachrymation. At first the lachrymation was serous in type, but soon it became yellowish, thicker, and almost purulent. The lids were tightly sealed and somewhat edematous. The symptoms continued to be fairly severe and the treatment was kept up for about a week. It was not until this time that the vision was at all clear. The lachrymation continued for some time.

Examination.—Slightly congested areas in the palpebral aperture on each side of the cornea. The conjunctiva showed slight thickening in the same exposed areas. The discharge resulting from the collection of the pus was found both in the inner and in the outer canthi. The palpebral conjunctiva showed nothing of significance.

CASE 6 (fig. 189).—Exposed 45 minutes in several shifts to strong concentration of mustard gas vapor, while wearing gas mask. The irritation of the eyes began at about 9 p. m., some five hours after exposure. There was severe burning and a feeling of sand and glass scratching in the eyes. There was profuse lachrymation and congestion. The next morning after the exposure the exudate from the eyes was seen to be more or less purulent and glued the eyelashes together and held the eyes closed. After the parts had been treated with cold boric acid compresses during the whole first night, as had been done in all the cases, it was necessary to "flush" the eyes with the solution in order to dissolve and loosen the plastic purulent exudate. When opened, the eyes were found to be much congested and small blebs were seen, especially on the lower palpebral conjunctiva. Argyrol was instilled as in the other cases and continuous compresses were applied for five days. The eyes were opened for short spaces of time on the fourth and fifth days and a blurring and dimness of vision was noted.

Examination.—Showed the same condition that had been found in the other cases. The acute congestion had decreased and the signs remaining were those of a somewhat chronic irritative process. There was the slight thickening in the exposed part of the bulbar conjunctiva in the palpebral fissure.

CASE 7.—Exposed directly to strong vapor. The vapor irritated the eyes severely and caused pain and lachrymation for 10 to 15 minutes. There were no blebs, but there was some congestion. After this there was no more pain and the patient continued to work where there was practically always some vapor. The patient's eyes were not painful but became more and more congested.



FIG. 188.—Dichlorethylsulphide conjunctivitis four weeks after exposure to vapor. In the acute stage there was extreme photophobia, lachrymation, pain, edema, and purulent exudation. The residual congestion and seropurulent exudation are still evident

Examination.—The whole conjunctiva was inflamed, congested, and slightly edematous, the lachrymation was increased in amount. The vision was apparently not involved. The bulbar conjunctiva was more markedly congested and affected than was the palpebral. Under the boric acid, continuous-compress treatment, there was a decided improvement, and the congestion was fairly well relieved in about four days. On the fifth day the area which was most markedly injected was in the bulbar conjunctiva of the palpebral fissure. Some of the scleral vessels in this region were injected. A small subconjunctival fatty area (pinguecula) was present.

CASE 8.—Exposed to fumes of ethyl alcohol, ethylene, and some dichlorethylsulphide. The eyes showed chronic irritation, thickening of the bulbar conjunctiva in the palpebral aperture, and some yellowish discoloration and areas that appeared to be fatty deposits. The patient complained of impaired vision and lachrymation. He previously had one severe arm burn, but there were no eye symptoms at that time.

CASE 9.—The patient had a slight irritation and itching and some congestion of the conjunctiva for about two weeks. At first the symptoms were very mild and noticeable only after exposure to dichlorethylsulphide. The symptoms were exaggerated and prolonged if the patient sat through a moving-picture show. Bright sunlight also increased the symptoms. The conditions were more or less cumulative and the symptoms gradually increased. During the second week he had lachrymation, congestion of the bulbar conjunctiva in the palpebral fissure and difficulty in accommodation in the right eye with more or less blurring of vision. There was also some sticky seropurulent exudate, and in the morning the eyelids and lashes were glued together, and a drop of pus was seen in the inner canthus. He used only the boric acid wash.

Examination.—He presented a picture similar to the previous cases, with a thickening of the conjunctiva of the eyeball that was exposed in the palpebral fissure. The right eye showed slightly more congestion and thickening than the left, and there was some ciliary injection about the scleroconjunctival junction. The palpebral conjunctiva, especially over the lower right eyelid, showed some congestion and slight thickening.

CASE 10.—Exposure without mask to strong concentration of mustard-gas vapor. Symptoms developed three hours later. He complained of severe irritation and pain in the eyes and the lids were swollen, edematous and could hardly be separated. The routine cold boric acid compresses were used, and it was not until three days later that the edema disappeared.

CASE 11.—Presented a somewhat different aspect. He was exposed for a few minutes to quite a heavy dose of dichlorethylsulphide vapor. He had some slight irritation and lacrymation, but no congestion to any marked degree. There was, however, a diminution of vision in the right eye which was said to be very marked. Both near and far vision were greatly reduced. There was blurring of all images.

Report of eye specialist.—"In regard to Case 11, whom I this day examined, I find his vision in right eye 4/200. Under atropine I find he has at least three diopters of hypermetropia, with some astigmatism, the correcting of which does not improve his vision. If this condition has been brought about in the last three weeks, as he claims, though the fundus does not show this, it must be toxic. Otherwise, it is amblyopie and his previous vision was not normal."



FIG. 189.—Dichlorethylsulphide conjunctivitis four weeks after exposure to vapor. The severity of the original process is indicated by the severe skin changes. The persistent congestion is the sole evidence of the severe conjunctivitis that was present

CASE 12.—Had been exposed to dichlorethylsulphide for about one month. He had some irritation and congestion about one week ago. The condition improved, but the patient complained of failing vision, dimness, and blurring. Both eyes were affected and the condition progressed rapidly; both near vision and distant vision were involved. The patient had to bring a printed page to within 6 inches of the eye in order to be able to read. A close examination of the corneae failed to reveal any opacities to account for the trouble. The corneal epithelium showed no apparent thickening or dulling. The conjunctiva showed some thickening and signs of chronic irritation in the part exposed in the palpebral fissure. It was considered that this case, like Case 11, was one of some internal fundus pathology or an accommodation disturbance.

CASE 13.—Exposure of one hour to very dilute concentration of mustard gas vapor. Six hours later, marked burning and irritation of conjunctiva, lacrymation, blurring of vision, and reddening of conjunctival surfaces. These symptoms lasted three days and gradually decreased, but a feeling of roughness of lids and visual disturbance persisted for nearly two months.

CLINICAL SUMMARY

From these cases it will be seen that exposure to varying concentrations of vapor of dichlorethylsulphide for varying periods produced a conjunctivitis showing all stages and degrees of intensity, from a simple acute type to a severe chronic proliferative conjunctivitis. The symptomatology and clinical picture varied greatly. The lesions were most marked in that portion of the bulbar

conjunctiva exposed in the palpebral fissure. The milder cases recovered after several days or weeks, but the more severe cases developed chronic hyperemia of the conjunctiva, new formation of vessels and scar tissue in the most severe, with more or less permanent disturbances of vision. One of the cases observed developed an almost complete amblyopia in one eye, so that only the perception of light and shadows was possible. In another case marked bilateral gradual reduction of vision was noted. A xanthomalike pigmentation was also noted in the chronic cases, the pigmentation developing near the outer or inner sclerocorneal junction, or over the corneal limbus.

There was no evidence of any metastatic involvement of the eye. In cases showing severe burns of other parts of the body, arm, leg, etc., no conjunctivitis, even of the simplest type, developed. Such exceptions are explained entirely by the fact that the vapor did not reach the eyes externally. In other cases, with severe burns over the entire body with the exception of the face, which was protected by the gas mask, no eye or conjunctival symptoms were noted.

CONCLUSIONS

1. The action of mustard gas upon the cornea and conjunctiva is essentially the same as that upon the skin. The conjunctiva is, however, less susceptible to the action, or better protected, as the degree of necrosis produced in it is always less than that in the cornea or the epidermis.

2. Exposures to dilute concentrations of the vapor produce slight degenerations of the corneal and conjunctival epithelium, followed by a simple conjunctivitis. The use of a 2 per cent alkaline aqueous fluorescein solution in demonstrating the necrosis of the corneal epithelium within 10 to 15 minutes after exposure to gassing has great clinical value.

3. Exposures to stronger concentrations produce a more or less complete necrosis of the corneal vertex, extending throughout the entire depth of the cornea. Purulent exudation into the anterior chamber may occur; but no changes except congestion and edema were observed in the posterior chamber or optic nerve in noninfected cases. In severe cases iridocyclitis and iritis may occur without secondary infection. The conjunctival epithelium also suffers necrosis, and there results an intense edema of the subconjunctival tissues with marked congestion, multiple hemorrhages, leucocyte infiltration, and frequently secondary liquefaction necrosis. The depth of the necrosis in the conjunctiva is much less than that in the palpebral epidermis. This difference in degree of escharization can be explained in part by the penetration of the hair follicles on the skin surface, and in part by the moistness of the conjunctival surfaces and the lachrymation. A diffuse mild inflammation of the peribulbar tissues occurs, often with marked infiltration of the ocular muscles. Purulent panophthalmitis may result from secondary infection, but is rare.

4. No metastatic lesions of the eye could be produced experimentally by applications of mustard gas to other regions of the body, or by subcutaneous or intraperitoneal injections.

5. For the milder forms of mustard-gas conjunctivitis immediate irrigation with the 0.5 to 1 per cent chlorcosane solution of dichloramine-T, followed by frequent irrigation with saturated boracic acid solution, is recommended; for the severe forms the same initial treatment, followed by frequent irrigations with the dichloramine-T alternating with boracic acid. We advise against the

use of bandages or compresses bringing pressure upon the eye, against the use of colloidal silver preparations, and against the use of cocaine. During exposure to mustard-gas vapor the dichloramine-T solution may be used as a prophylactic agent.

6. Healing in the more severe forms results in vascularization and cicatrization of the cornea with marked disturbances in vision. Even in the milder forms of conjunctivitis, localized roughness or irregularity in the conjunctival surface may persist for weeks as the result of localized edema, hyperemia, cellular infiltration, etc. Serious refractive errors and reduction of vision result, even in mild cases. For the correction of the disturbances of vision the patient should be referred to a competent specialist.

LESIONS OF THE RESPIRATORY TRACT

METHOD

In the gassing investigations use was made of a simple apparatus which served our purposes most effectively and is to be recommended for its simplicity as well as for the relative accuracy with which the gas concentration could be estimated. As shown in Figure 190, it consisted of:

A. One or more bottles containing sulphuric acid for drying the air admitted.

B. A container for the liquid mustard gas so arranged as to be easily detached from the tubing, so that when stoppered with a ground-glass stopper it could be weighed with its contents. Above this was a shunt tube for varying the amount of pure air admitted to the chamber, thus varying the concentration of gas obtained. Within the mustard gas bottle strips of absorbent paper were so arranged as to increase the evaporation surface. When used for experimental work with toxic substances, which are gaseous at room temperature, the gas intake replaced this weighing bottle.

C. A gassing chamber which was large enough to hold several small animals or a large dog. It had a removable plate-glass top, so that the animals could be observed during gassing; this was sealed during the experiment with the gutta-percha-tallow mixture, commonly used for making air-tight seals for museum jars, and could be held in position by a heavy weight if necessary.

D. and E. Bottles for removing the gas from the air flowing from the chamber, so that the amount passing over could again be estimated here if desired. When used for mustard gas these bottles might contain a chlorinated solution for the destruction of the gas.

F. A standard gas meter for measuring the amount of air passing through the chamber.

G. A suction pump attached to the city water supply.

After detaching the weighing bottle, air was drawn through the gassing chamber for some time in order to wash out the mustard or other gas remaining. The weight of mustard gas used was obtained by difference, and the amount of air drawn through during the period in which the bottle was attached was recorded from the gas meter. The concentration represented by these figures was obtained by reference to a transformation table. The results were as approximately correct as could be obtained by any form of gassing chamber, and the apparatus had the advantage of simplicity. As far as mustard gas is concerned,

such factors as variable absorption by the hair of the animal, etc., introduce unavoidable errors, so that absolute accuracy of method could not be obtained regardless of the limitations of the apparatus.

The animals were killed by a direct blow upon the neck, to avoid the changes in the respiratory system produced by an anesthetic. Autopsies were made as quickly as possible after the death of the animal. The tissues were fixed in formol, embedded in paraffin, and the usual stains, such as hematoxylin and eosin, were employed.

GROSS AND MICROSCOPIC PATHOLOGY

Various series of animals were exposed to varying concentrations of mustard gas in the gassing chamber for varying periods of time. It was found that rabbits would survive a 40-minute exposure to a dilution of 1:110,000, recovery taking place after a period of respiratory involvement. For purposes of brevity, typical protocols have been selected and are given here.

PROTOCOLS

RABBIT 32.—Exposed in the gassing chamber for 40 minutes to a 1:110,000 concentration. During the gassing the rabbit frequently changed position, rubbed its nose, and showed

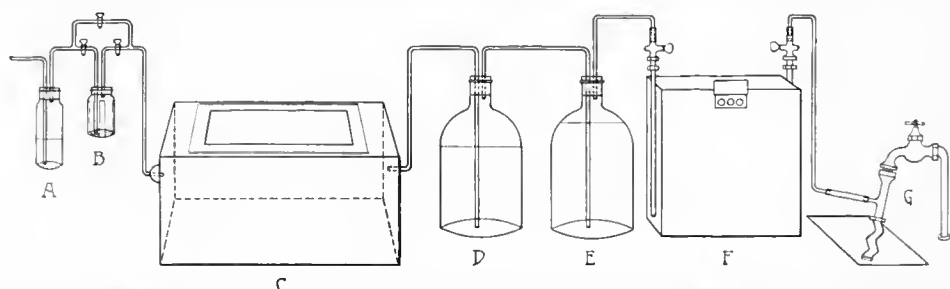


FIG. 190.—Experimental gassing apparatus. Pathological laboratory, University of Michigan. A, washer containing sulphuric acid; B, gas container; C, gassing box; D and E, degassing bottles; F, standard gas meter; G, suction pump

signs of irritation. When removed from the gassing chamber the rabbit appeared unaffected in any way. In two and one-half hours conjunctival erythema and increased lacrymation were evident, these symptoms increasing until the animal was killed. Seven and one-half hours after removal from the box, symptoms of coryza manifested themselves. Twelve hours after removal from gassing chamber, rabbit was killed by blow upon the neck. The conjunctivae presented marked congestion and edema, and were covered with purulent flakes. The bulbar conjunctivae showed a marked collar of edema at the limbus. The cornea showed a slight haziness, and at its vertex there was a definite necrosis of the superficial epithelium. This area was irregularly oval in shape. The lid margins showed congestion and the skin about mouth and nostrils was erythematous.

Autopsy showed right-sided dilatation of the heart. No fluid was found in the pleural cavity, and there were no pleural changes. On section the lungs showed marked congestion and edema without hemorrhages or atelectasis visible to the naked eye. No differences between upper and lower lobes were noted. The trachea was filled with frothy mucus and the mucosa was congested, particularly in the upper portion, the congestion diminishing below toward the bronchi. The mucosa of the entire upper respiratory tract, nose, mouth, pharynx and larynx showed congestion without hemorrhages.

Microscopic findings.—Nose: Sections from the skin about the nostrils showed slight pyknosis of the epidermis and congestion of the vessels, without other changes. The mucous membrane of the nose showed a marked congestion, more marked pyknosis of the epithelium and slight edema. Sections from the pharynx and larynx showed a marked congestion with extreme mucous degeneration of the mucous glands. There was pyknosis of the upper layers

of the epithelium of the mucous membrane but no definite necrosis. The acini of the mucous glands were greatly enlarged and filled with deep blue-staining mucus. The ducts were dilated and filled with mucus. There was but slight edema of the mucous membrane and no hemorrhages. These signs diminished in the trachea except for the edema, which was somewhat greater in the lower part of the trachea than above, and there was an increased number of wandering cells in the mucosa. The columnar cells of the tracheal mucosa showed more marked changes than the squamous epithelium of the upper respiratory tract. The great majority showed a hydropic or a mucoid degeneration. The epithelium was intact for the greater part but small patches of desquamation occurred. The larger bronchi presented the same appearance as the trachea, though to a somewhat lesser degree. The smaller bronchi were filled with mucus. The epithelium showed mucoid degeneration and occasional areas of desquamation. The walls of the larger bronchi were edematous, the vessels markedly congested, but there was no increase in leucocytes. The exudate in the bronchi was entirely mucoid or albuminous in character, not fibrinous. There was no hemorrhage into the bronchi.

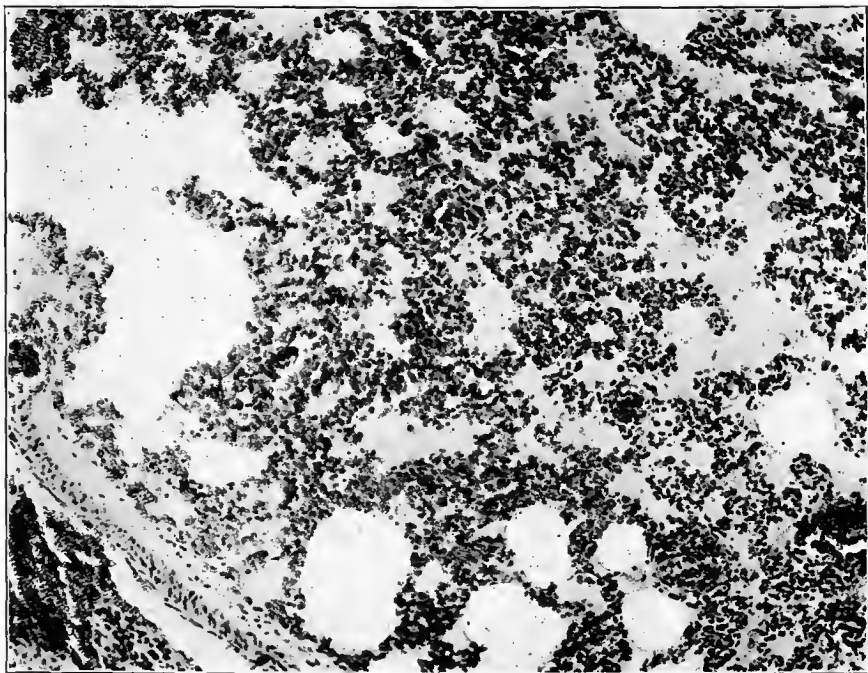


FIG. 191.—Rabbit. Exposed 40 minutes to a 1:110,000 concentration. Killed 12 hours after removal from gassing chamber. Section of lung. Marked congestion, edema, and area of partial atelectasis alternating with those of emphysema

The lung tissue showed extreme congestion and marked edema with numerous minute hemorrhages, too small to be seen with the naked eye. (Fig. 191.) A majority of the alveoli were filled with a heavy albuminous precipitate, but scattered throughout the lung were numerous emphysematous alveoli and dilated bronchioles. No areas of complete atelectasis were seen, although edematous areas showed partial collapse.

The changes in the respiratory tract of this animal were those of an acute catarrhal rhinitis, pharyngitis, laryngitis, tracheitis, and bronchitis, decreasing somewhat in intensity from above downward, with pulmonary congestion and edema.

RABBIT 33.—Exposed 20 minutes to a concentration of 1:15,000. During the exposure the rabbit changed its position from that of facing the inflowing mustard gas to the opposite direction. Three hours after removal from the gassing chamber the animal showed increased lacrymation in both eyes. The borders of the eyelids, skin areas about the mouth and nostrils, the ears and all parts of the body where the hair was short and thin exhibited

a marked erythema. The animal showed marked photophobia and irritation of the eyes. Eight hours after removal from the chamber flakes of purulent material were seen over the conjunctivæ and a definite coryza had developed. The conjunctivæ were edematous and congested. These symptoms increased for 36 hours, when the animal was killed.

Autopsy showed a severe conjunctivitis and coryza. Right-sided dilatation of the heart. The upper air passages were filled with foamy exudate and the mucosa was congested. Pleural cavities and pleuræ negative. The lungs were markedly congested, the right lung more so than the left. The lungs appeared air-containing throughout, except for the middle lobe on the right, which was solid in areas, dark red in color. On section it bled but slightly. Beyond congestion no other changes were found in any organs or tissues.

Microscopic findings.—The cutaneous borders of the nostrils showed necrosis, edema, congestion and marked leucocyte infiltration of the corium. The mucous membrane of the nose presented patches of necrosis of the epithelium, congestion and edema, areas of small-

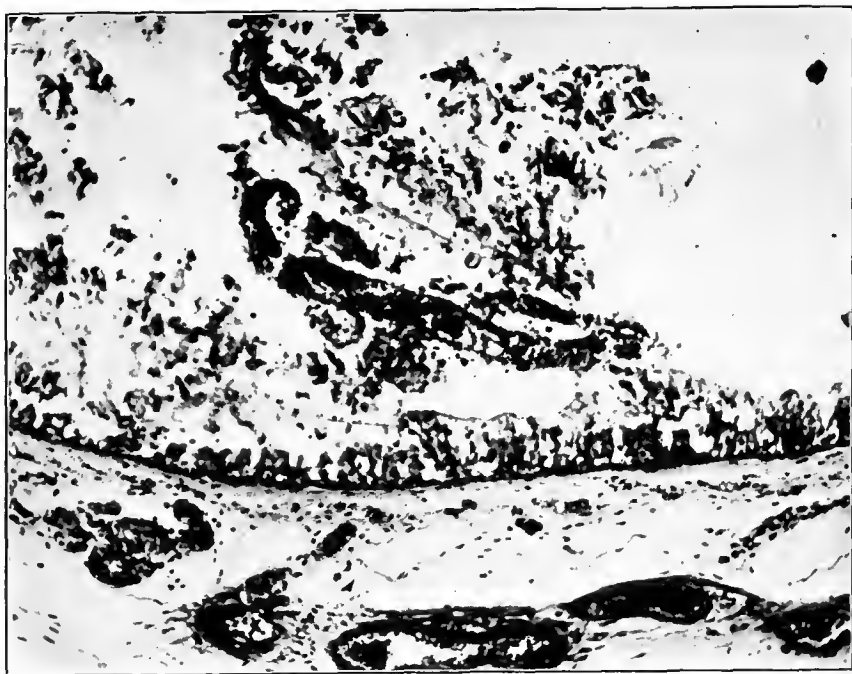


FIG. 192.—Exposed 20 minutes to a concentration of 1:15,000. Killed 36 hours after gassing. Section of trachea showing acute catarrhal desquamative tracheitis; marked mucoid degeneration of the epithelium; congestion and edema of the submucosa. Lumen filled with mucous containing many desquamated cells

celled infiltration of the submucosa, and marked mucous degeneration of the mucous glands. Mouth and pharynx: Sections of tongue and pharyngeal wall showed a contraction of the upper half of the squamous epithelium with pyknosis of the nuclei, congestion of the vessels, slight edema of the submucosa and slight small-celled infiltration. The larynx presented patches of necrosis in the hyperemic mucous membrane, with marked edema extending to the cartilages. Small-celled infiltration was well marked. Mucous glands showed mucoid degeneration. The surface of the mucosa of the trachea was covered with patches of mucus containing desquamated cells. The epithelium showed marked mucoid and hydropic degeneration; there were large areas of complete necrosis with desquamation. In the submucosa there was a marked edema extending to the cartilage rings. The vessels were markedly congested (Fig. 192). The larger bronchi showed marked degeneration and necrosis and desquamation of the epithelium, the epithelium being represented for the greater part by a single line of nuclei at the base. Many of the bronchi were filled with an exudate of mucus containing many desquamated and degenerating cells but few leucocytes. There was some edema of the walls of the bronchi and the number of leucocytes was increased around the bronchi. The smaller bronchioles showed a better preserved mucous membrane

but many of the cells were vacuolated, presenting mucoid or hydropic degeneration, and desquamation was frequent. The lung showed practically the same picture as in the preceding; marked congestion and edema, small hemorrhages into the alveoli and emphysematous alveoli and dilated bronchioles. Many of the edematous areas showed partial atelectasis. The apparently solid area from the right lung presented a more marked atelectasis and a greater degree of edema but no pneumonia. Other organs showed marked congestion without other changes.

The microscopical picture in this case was similar to that in the preceding, but the changes were somewhat greater in intensity with a greater degree of necrosis and a well-defined leucocyte reaction.

RABBIT 30.—Exposed 30 minutes to a concentration of 1:15,000. Killed $4\frac{1}{4}$ days after removal from the gassing chamber. Within 5 minutes after removal from the box the animal showed the first signs of irritation, rubbing its eyes and nose frequently. Six hours afterwards there was a well-developed conjunctivitis. By 24 hours the conjunctivitis had

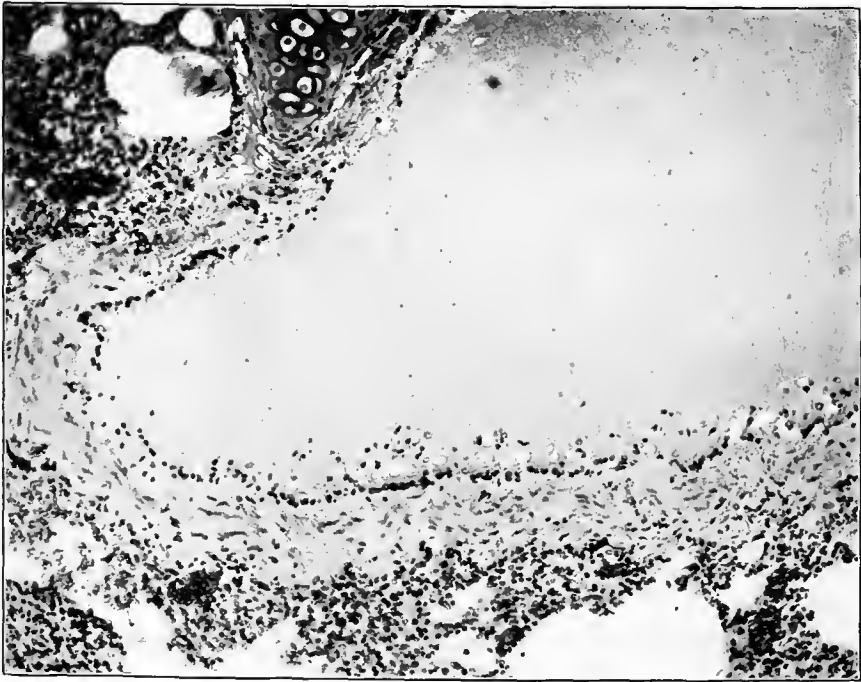


FIG. 193.—Rabbit. Exposed 30 minutes to a concentration of 1:15,000. Killed $4\frac{1}{4}$ days after gassing. Section of larger bronchus showing lumen filled with edema fluids. Bronchial epithelium shows marked mucoid and hydropic degeneration

greatly increased, with marked conjunctival edema, and the animal showed a marked bilateral coryza. By the second day the snuffles and coryza were much worse, the animal showing a marked respiratory wheezing, audible several feet away. The conjunctivitis had become distinctly purulent in character, with multiple subconjunctival pin-point hemorrhages, extreme edema and beginning corneal ulceration. Throughout the day the snuffles and wheezing greatly increased, the animal appeared sick, restless, with respirations greatly increased and shallow, these symptoms reaching their height in the evening of the second day. From the morning of the third day the respiratory symptoms gradually improved until the animal was killed, $4\frac{1}{4}$ days after gassing.

Autopsy.—The eyes showed a very severe purulent conjunctivitis, with characteristic porcelain appearance of the cornea. The mucosa of upper respiratory tract showed marked congestion and edema and mucous exudate, diminishing in intensity from the nostrils to the nasopharynx. In the anterior 2 cm. of the nasal tract the exudate was purulent in character. The nasopharynx, larynx, and trachea presented marked congestion of the mucosa, and the lumen of the trachea was filled with a frothy mucus extending into the bronchi. No hemor-

rhages or ulcerations were seen in the mucosa of the upper respiratory tract. Pleural cavities and pleuræ were negative. The lungs were uniformly markedly congested and apparently air-containing throughout. No pneumonic areas or hemorrhages could be felt or seen. The heart presented a marked right-sided dilatation. Beyond a marked congestion, other organs and tissues showed nothing.

Microscopic findings.—Nose: Sections from the anterior nostrils showed a marked necrosis and ulceration of the mucosa with a marked edema and congestion of the submucosa and a polynuclear infiltration. Great numbers of staphylococci were seen on the necrotic mucosa. Throughout the submucosa were numerous minute hemorrhages by diapedesis, and in one medium-sized blood vessel a definite thrombus. The mucous glands showed the squamous epithelium to be intact for the greater part, but the outer half was necrotic, dry, looking like stratum corneum. Larynx: The surface epithelium was completely necrotic in many areas, particularly where a mucoid exudate lay upon the surface. In other areas it was preserved, but had lost its columnar appearance, and was reduced to a layer of pyknotic nuclei staining almost black with hematoxylin. In the mucoid exudate in the lumen there

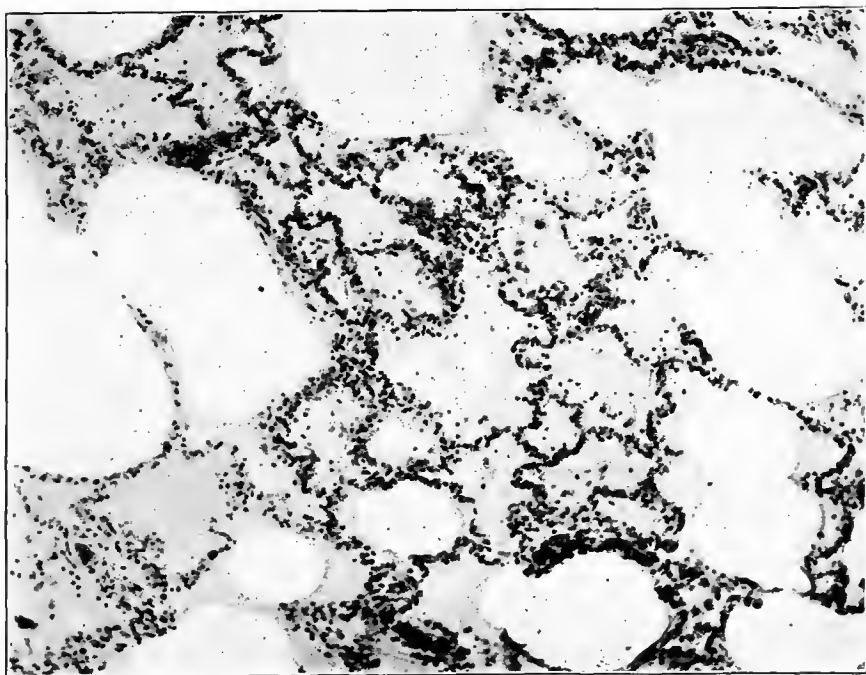


FIG. 194.—Lung of same rabbit as Figure 193. Acute congestion and edema

were great numbers of swollen desquamated mucoid epithelial cells and very few leucocytes. The submucosa was edematous, the edema, however, being very irregularly distributed. The blood vessels showed marked congestion and the number of leucocytes in the submucosa was not increased. The laryngeal mucous glands showed marked mucoid degeneration. Many of the larger bronchi were filled with mucus. The columnar cells showed marked mucoid degeneration and pyknotic nuclei. Practically every cell was converted into a goblet cell. There was no increase of leucocytes in or about the bronchi. The pulmonary vessels showed extreme congestion and in many of these were large masses of fibrin, irregularly scattered through the red blood cells, or at times somewhat laminated, presenting the appearance of recent thrombosis. Throughout the lung atelectatic areas alternated with emphysematous. The alveolar spaces of the atelectatic areas showed marked edema, being filled with a pink-staining finely granular precipitate. The bronchioles in these atelectatic areas were distended and were filled with either a similar edematous fluid or a more mucous fluid. No pneumonic areas were found and no large hemorrhages. Minute hemorrhages by diapedesis were found along the walls of the greatly distended capillaries. The other organs showed nothing but intense congestion. (Figs. 193, 194.)

The lesions were practically the same as in rabbit 33, except that they were more severe in the nose and mouth. The purulent character of the nasal lesions was probably to be explained by the development of a secondary infection due to a staphylococcus.

RABBIT 31.—Exposed 35 minutes to a concentration of 1:30,000. On removal from the gassing box the animal showed some irritation of the eyes and nose. Four hours after removal the animal had developed a well-marked conjunctivitis, with erythema of the exposed skin surfaces and beginning snuffles with scant nasal secretion. Within 24 hours there was marked increase of conjunctivitis and coryza. The animal was killed 30 hours after gassing.

Autopsy.—Eyes showed a marked conjunctivitis, with purulent exudate. Exposed skin surfaces showed erythema and edema. The mucosa of entire respiratory tract from nose to bronchi showed congestion, slight edema, and abundant mucous exudate. Pleural cavities negative. Pleurae negative. Lungs presented uniform congestion without consolidation, the lung tissue being apparently air-containing throughout. No hemorrhage or atelectatic or pneumonic areas visible to the naked eye. The heart showed dilatation of the right side. In other organs nothing notable but congestion.

Microscopic findings.—Nose: Squamous epithelium of the anterior nostrils showed patches of complete necrosis, these minute erosions or ulcerations being covered with a fibrinopurulent exudate. The remaining epithelium showed more or less pyknosis. There was very little edema of the submucosa and no small-celled infiltration or hemorrhages. On the skin side of the nostrils the edema was more marked than on the mucosal side, and there was marked necrosis, pyknosis, and desquamation of the epidermis. Pharynx: Squamous epithelium of mouth and pharynx showed patches of pyknosis, contraction of the upper third with pyknosis of the nuclei resembling cornification, congestion of the blood vessels and slight edema of the submucosa. Larynx: The columnar epithelium showed marked mucoid or hydropic degeneration. The majority of the cells of the upper layer were either vacuolated or were goblet cells. The nuclei stained very heavily, but the epithelium was for the greater part intact, without desquamation. In the lumen there was a thin albuminous fluid containing very few desquamated cells, leucocytes, no fibrin, and but a small amount of mucin. The submucosa showed a rather marked edema with the leucocytes slightly increased. The vessels were markedly congested. The mucous glands showed increased mucus formation. Trachea: The epithelium was intact throughout the greater portion, but showed mucoid and hydropic degeneration. The lumen was filled with a thin mucoserous fluid. Well-marked edema of the submucosa with some increase in leucocytes. Marked congestion of the vessels. Bronchi: The lungs presented practically the same appearance as in the previously described cases but with less edema and on the whole a less marked congestion. The bronchi contained a smaller amount of fluid. The epithelium was better preserved, although showing mucoid change and vacuolar change in the larger ones. There was very little atelectasis, the lungs being rather emphysematous throughout. There was no pneumonia and no hemorrhage. The other organs showed chronic congestion. The liver a chronic coecidiosis with cirrhosis. (Figs. 195, 196.)

In this rabbit the lesions in the anterior nares were severe, the degree of necrosis there being comparable to that on the conjunctiva and cornea, but the laryngeal, tracheal, and bronchial lesions were of the mildest degree.

RABBIT 46.—Gassed six hours at a concentration of 1:50,000. Animal died 60 hours after removal from the gassing chamber. During the gassing the animal showed irritation within half an hour. At the end of an hour it became drowsy and was quiet, with its eyes half closed. Within three hours there was a definite lachrymation and conjunctival edema, these conditions increasing during the remainder of the gassing. When taken from the box the eyes were very much congested, edematous, and showed profuse lachrymation. By the next day the rabbit showed marked respiratory involvement, coughing all the time, and bubbling râles could be heard throughout its chest. These conditions increased during the next 2 days, the animal dying 60 hours after removal from the gassing chamber.

Autopsy.—Both eyes presented marked corneal opacity with mucopurulent conjunctivitis. Pharyngeal mucosa very markedly congested and edematous and covered with mucopurulent exudate. Buccal mucosa negative in appearance. Marked edema of all

laryngeal structures and tracheal mucosa, the tracheal edema being most marked in the upper part, just beneath the larynx, where there were also small hemorrhages in the mucosa. Pleural cavities and pleuræ negative. Pericardial fluid increased, clear. Heart dilated; both sides filled with partly clotted blood. Both lungs were voluminous and air-containing without any airless areas except a small atelectatic area in the border of the lowest left lobe. On section the lungs showed moderate congestion and edema without any hemorrhages or pneumonic or atelectatic areas visible to the naked eye. Other organs showed no changes except congestion.

Microscopic findings.—Nose: Anterior nares showed a shrinking and pyknosis of the epithelium, the outer layers being desquamated and light staining, resembling cornified epithelium with pyknotic nuclei. In many areas this pyknosis and shrinking extended to the lowest layer of the epithelium. Through the lowest layer there were many hydropic cells and occasionally small vesicles were formed. The ciliated columnar epithelium showed a more marked necrosis, vacuolization and desquamation. There was marked edema of the

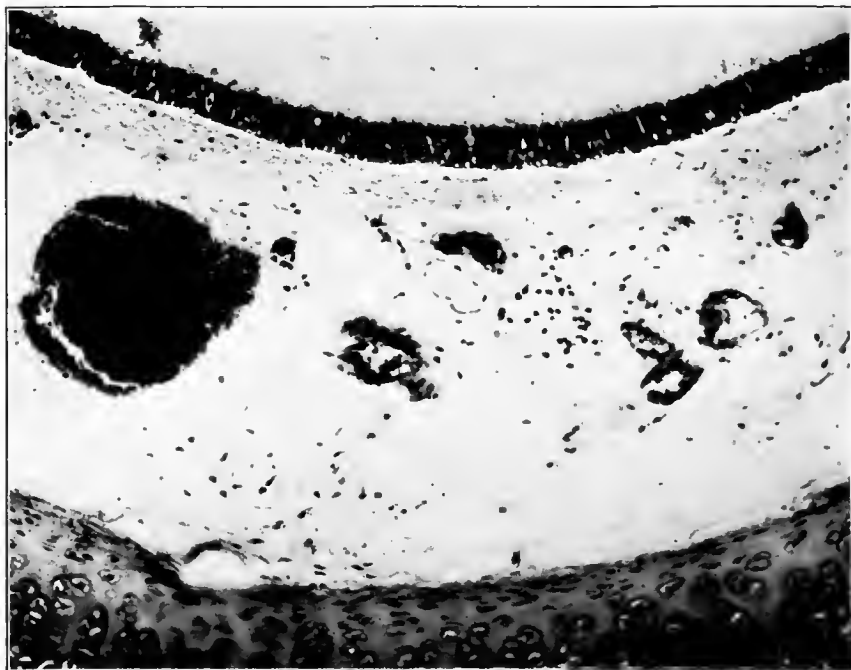


FIG. 195.—Section of laryngeal mucosa of rabbit. Exposed 35 minutes to a concentration of 1:30,000. Killed 30 hours after gassing. Pyknosis and mucoid degeneration of the epithelium. Marked congestion and edema of the submucosa

submucosa extending to the cartilages and through the muscles. The mucous glands showed extreme mucoid degeneration; the blood vessels, extreme congestion. There were minute hemorrhages about the mucous glands and the number of wandering cells was increased. The buccal mucosa and the tongue showed necrosis of the upper half to two-thirds of the squamous epithelium, with partial desquamation of these dead cells in lamellæ. There was slight edema and moderate congestion of the subepithelial tissues. The mucosa of the pharynx showed the same changes with a more marked edema of the submucosa. Larynx: In the lumen, lying upon the surface, there was a fibrinopurulent membrane which was firmly attached in areas where the epithelium was completely lost. In these areas the picture was that of a diphtheritis. Colonies of staphylococci were present in the diphtheritic membranes and on the necrosed epithelium. Where the epithelium was preserved it showed marked vacuolation with hydropic and mucoid degeneration. In some areas the epithelium was still attached but was necrotic and infiltrated with polynuclears and eosinophile cells. There was a very marked subepithelial edema, extreme congestion of the blood vessels and

areas of leucocyte infiltration, many of these being eosinophiles. This infiltration was most marked in the neighborhood of the diphtheritic areas. The cervical lymph nodes in this case showed marked eosinophilia and great numbers of hemophages in the sinuses. Trachea: Mucosa of the trachea showed marked mucoid and hydropic degeneration. There was a diphtheritic necrosis, but the process was less marked than in the larynx. Edema and congestion of the wall were about the same. Bronchi: The epithelium of the larger bronchi showed marked degeneration and necrosis. There was an increase in leucocytes in the walls of the larger bronchi, the submucosa was edematous and the vessels were markedly congested. The majority of the smaller bronchioles contained a mucopurulent exudate and the bronchial wall was infiltrated with leucocytes. Around many of the bronchioles there were definite areas of a hemorrhagic purulent bronchopneumonia. Colonies of staphylococci were found in each of these areas. Between these areas the alveoli were overdistended and emphysematous. Other alveoli contained a heavy albuminous precipitate of edema. The liver presented a marked nutmeg liver, central necrosis and congestion of lobules. The kidneys showed marked cloudy swelling and congestion. (Figs. 197, 198.)

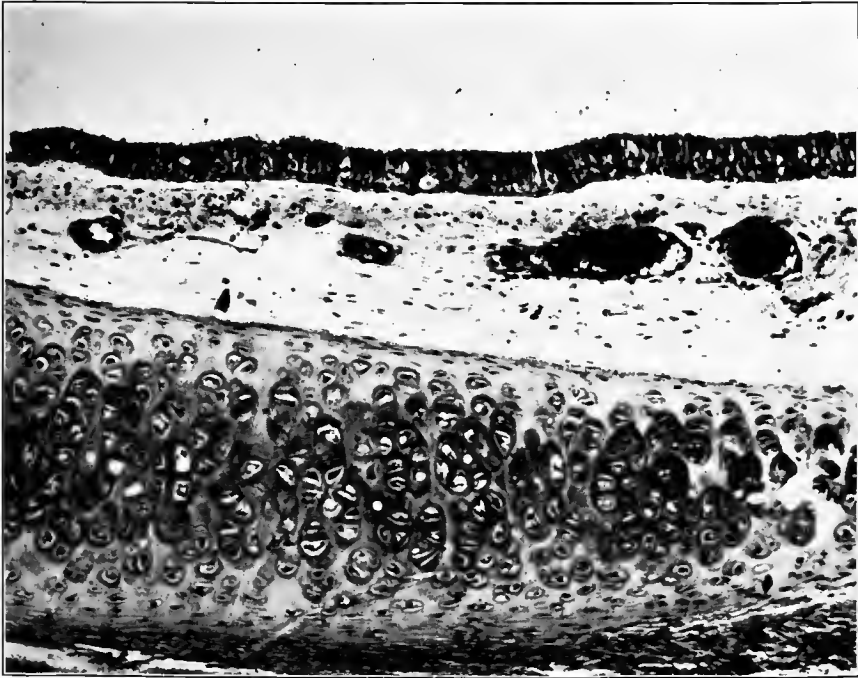


FIG. 196.—Section of tracheal wall of same rabbit as Figure 195. Similar changes in epithelium and submucosa

The respiratory lesions in this animal were more pronounced than in any of the preceding, as was shown by the diphtheritic necroses in the larynx and trachea, the purulent bronchitis, and bronchopneumonia. The cause of death was considered to be an infective (staphylococcus) bronchopneumonia, secondary to the lesions produced by the gassing.

RABBIT 45.—This rabbit was gassed at the same time as rabbit 46, in the same box, for six hours at a concentration of 1:50,000. Its reaction during the gassing and afterwards appeared to be identical with that of No. 46, but the animal lived for seven days.

Autopsy.—The autopsy findings were the same as for No. 46, but the changes were more severe in character. The anterior nares showed extensive ulcers covered with diphtheritic membrane, and the nasal cavity was filled with a mucoid fibrinopurulent membrane, this membrane extending through the nasopharynx and into the larynx and trachea. This membrane was in part firmly adherent to the wall, particularly along the posterior wall,

while anteriorly it was loose and separated as a cast of the tracheal tube. Heart showed marked dilatation of both cavities. Pleurae and pleural cavities negative. Large bronchi filled with purulent exudate. Lungs voluminous, markedly congested and edematous, with the picture of a diffuse bronchopneumonia.

Microscopic findings.—The microscopic examination of the nose, nasopharynx, larynx, and trachea revealed the presence of a diphtheritic inflammation, with a membrane containing numerous colonies of cœci. This membrane was firmly attached wherever the epithelium was completely lost, but was loose and separated from the surface wherever the epithelium was still intact. In the larynx and trachea a large part of the columnar epithelium was replaced by a regenerating layer of large, deeply staining pavement or euboidal cells. The submucosa showed marked congestion, edema, scattered hemorrhages, and leucocyte infiltration. The larger bronchi were filled with a fibrinopurulent membrane which was adherent to the wall and contained many large colonies of cœci. The epithelium was entirely absent except in a few places where there was a regenerating layer. Lungs: The lungs presented

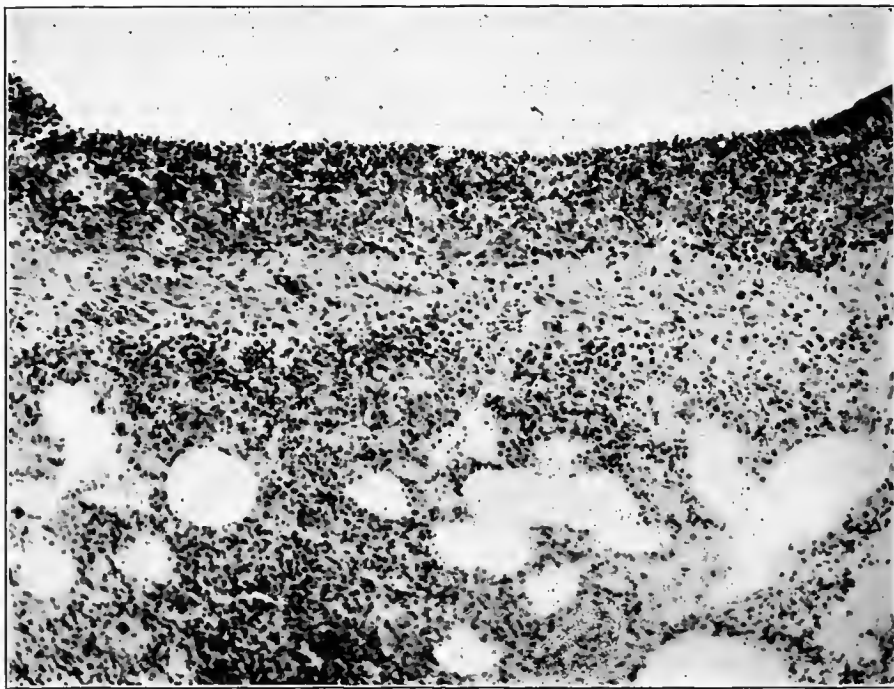


FIG. 197.—Exposed six hours to a concentration of 1:50,000. Died 60 hours after gassing, section of large bronchus, showing purulent necrotic bronchitis

the picture of an advanced fibrinopurulent bronchopneumonia with large areas of consolidation. All of the bronchioles appeared as abscesses. In some of these there were many large epithelial giant cells, syncytial in type, showing an attempt at regeneration, but the great majority showed complete destruction of the epithelium. Syncytial epithelial giant cells were also found in some of the alveoli. Colonies of cœci were found everywhere. Many of the pneumonic areas showed older and fresh hemorrhages and marked inflammatory edema. (Figs. 199, 200.)

This case presented a more marked diphtheritic inflammation of the upper respiratory tract and a diffuse purulent bronchopneumonia due to secondary infection following gassing.

RABBIT 43.—Exposed for 12 hours to a concentration of 1:50,000. Died 54 hours after removal from the gassing chamber. In the first stages of the gassing the animal showed nasal irritation, but later became drowsy and depressed, and sat with eyelids nearly closed. At the end of two hours increased lachrymation and conjunctival edema were first noted.

When removed from the gassing chamber there was a well-marked conjunctivitis, with coryza and salivation. The animal would not eat or drink, but appeared stupefied. The coryza gradually increased in intensity and within 6 hours after removal from the chamber bubbling respiratory sounds were heard over its thorax. Coryza and conjunctivitis increased during the first 24 hours, at which time there was a profuse seropurulent nasal discharge. The wheezing and bubbling respiratory sounds could be heard some distance from the cage. Respirations were rapid and apparently difficult. Thirty-six hours after gassing the rabbit was still much depressed and the respiratory sounds were louder. The animal frequently sneezed and coughed. There was a marked purulent discharge from the eyes and nose. Forty-eight hours after removal from the gassing chamber the animal was very weak, the respiratory movements more rapid and much forced, the thorax heaving. Both eyes were sealed with a thick purulent exudate. After increasing respiratory difficulty the animal died, 54 hours from the time of exposure.

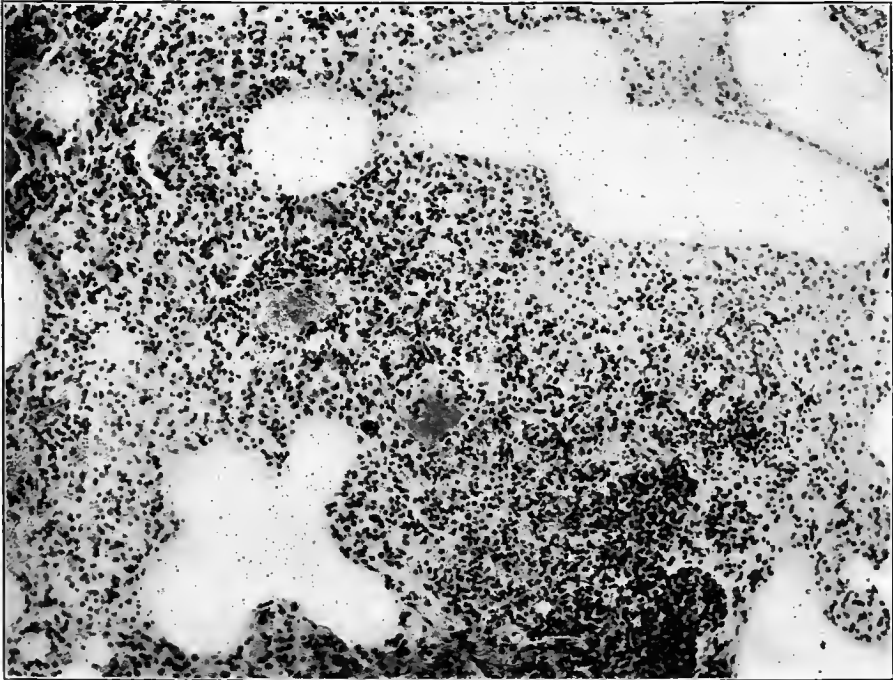


FIG. 198.—Section of lung from same case as Figure 197. Area of purulent bronchopneumonia with colony of cocci in the center of the field

Autopsy.—Marked purulent conjunctivitis with corneal ulceration. Erythema of the exposed portions of the skin. Marked edema of the subcutaneous tissue, particularly in the region of head, neck, and thorax. Nose filled with purulent exudate, the mucosa showing deep necroses. Nasopharynx filled with mucopurulent fluid. Larynx and trachea filled with frothy exudate beneath which there was a membranous cast, partly adherent but decreasing in intensity downward. The mucosa of the entire upper respiratory tract was markedly congested and showed marked necrosis of the surface epithelium. The lungs showed marked congestion and edema. At the base of each lung there was an olive green area, the central portion of which was lighter in color. Bronchi filled with a thick mucopurulent exudate. Pleurae were negative. Heart showed marked dilatation of the right ventricle. All other organs showed marked congestion. Some cloudy swelling in the kidneys. The external genitals were very erythematous and edematous.

Microscopic findings.—The nose was filled with a diphtheritic fibrinopurulent exudate and the epithelium was completely necrosed, except for very small areas in the folds. The membrane was for the greater part adherent, but loosened in some areas. The submucosa showed marked congestion, leucocyte infiltration, and edema, extending into the muscles

and cartilages. The mucosa of the pharynx showed a more marked necrosis of the squamous epithelium than in any of the above cases. The cells of the lowest layers were markedly pyknotic. The larynx and the trachea showed a diphtheritic process, the surface being covered with a fibrinopurulent membrane which was firmly attached where the epithelium was entirely absent, but lying loosely on the surface where the epithelium was still intact or regenerating. In the membrane there were colonies of cocci. The epithelium of the larynx and trachea was reduced to a single layer of pyknotic nuclei over a large extent of surface. The submucosa showed marked fibroblastic proliferation, leucocyte infiltration and edema, with minute hemorrhages. The mucous glands of the larynx and trachea showed some acini and ducts distended with mucus, but the greater number of the acini appeared small, collapsed, and pyknotic. The inflammatory infiltration and edema extended into the muscle. The mucosa of the upper part of the esophagus showed marked pyknotic nuclei and necrosis of the upper layers of the epithelium. The large bronchi showed a nearly complete necrosis of the

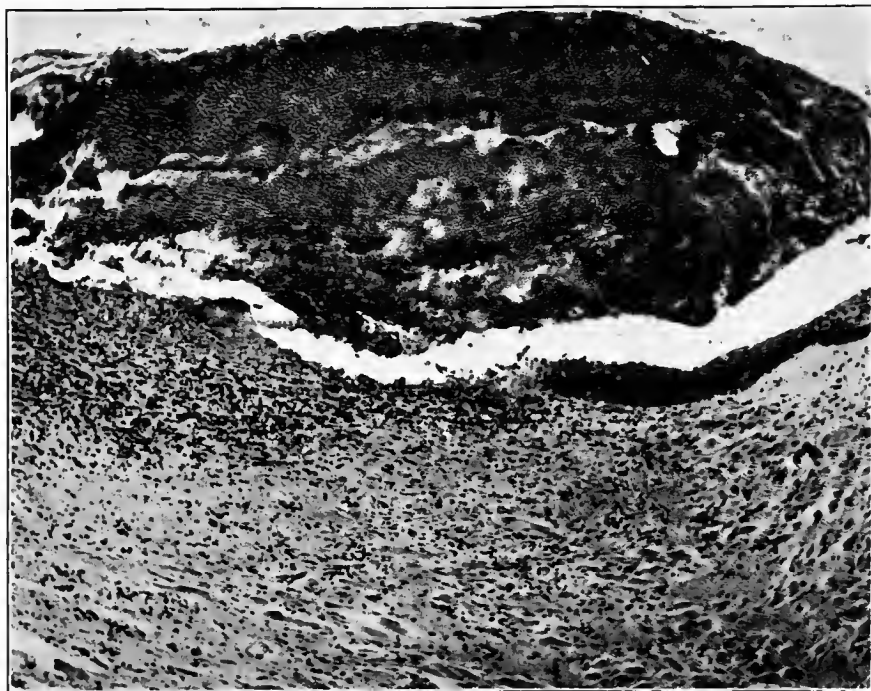


FIG. 199.—Rabbit. Exposed for six hours to a concentration of 1:50,000. Died seven days after gassing.
Eschar from upper portion of larynx

epithelium and a fibrinous membrane adherent to the surface forming casts of the bronchial tubes. There was marked congestion of the wall and leucocyte infiltration of the surrounding tissues. The smaller bronchioles were filled with mucous and albuminous exudate with increased leucocytes. The epithelium was intact, but showed mucoid degeneration and pyknotic nuclei. A very few bronchi contained a mucopurulent exudate. The lungs showed extreme congestion, numerous hemorrhages by diapedesis, a few small areas of early bronchopneumonia and atelectatic edematous areas beneath the pleura. The only bacteria found were those in the bronchioles containing the mucopurulent exudate. Marked congestion of all other organs. Cloudy swelling of the liver and kidney cells.

This case differed from the preceding in the severe diphtheritis of the upper respiratory tract with more marked evidences of healing in the larynx and trachea. It showed a severe secondary infective process of the larynx and trachea with less involvement of the bronchi and lungs.

RABBIT 44.—Gassed for 12 hours at a concentration of 1:50,000, at the same time with rabbit 43. Reaction during the gassing identical. Developed a corresponding conjunctivitis and coryza with similar pulmonary symptoms. This animal, however, survived until 92 hours after the end of the exposure.

Autopsy.—Generalized mustard-gas burn of the skin, especially where the hair was thin, in the form of a marked erythema, marked subcutaneous edema and dilatation of the superficial vessels. The untreated left eye showed a severe purulent conjunctivitis with corneal opacity and superficial ulceration. The right eye had been treated with dichloramine-T and showed a much less severe conjunctivitis and injury to the cornea. The upper respiratory tract was filled with frothy exudate. The mucosa, particularly of the trachea, showed a diphtheritic necrosis with membrane, most marked at the larynx and just below it, but extending into the bifurcation. Bronchi filled with frothy exudate. The lungs were voluminous, with marked congestion and very edematous on section. Atelectatic areas seemed to alternate with emphysematous. At the anterior border of the lowest lobe of the left lung, there was



FIG. 200.—Same rabbit as Figure 199. Section of larynx showing diphtheritic ulcer

an area greenish gray in color, softened and apparently necrotic. Right ventricle and conus markedly dilated. All other organs congested. In the intestine, small necrotic areas, with inflammatory reaction about them, were found, the entire intestine being markedly congested.

Microscopic findings.—Nose: Slough of the skin of the nose adherent. On the mucous membrane side was an ulcer with slough adherent in some areas. Fibroblastic proliferation well developed. Mouth: Tongue showed numerous small areas of ulceration and sloughs extending down to the muscle. The remaining portion of the epithelium was intact but showed pycnosis and contraction of the outer half. Pharyngeal mucosa showed the same lesions. Mucous glands of nose and nasopharynx showed very marked mucoid degeneration. Intense congestion of the neighboring vessels. Patches of leucocyte infiltration. The larynx showed a purulent infiltration of the wall extending to the cartilages. A fibrinopurulent membrane was adherent to the surface over the greater portion and beneath the membrane there was a phlegmonous infiltration of the wall of the larynx. Small patches of epithelium upon the surface had the appearance of regenerating epithelium, regeneration taking place apparently from the ducts of the mucous glands. Numerous colonies of cocci

were found in the pus. Below the larynx the epithelium was present over the greater part of the tracheal mucosa, which showed mucoid and hydropic degeneration. There were also islands of regenerated epithelium with some fibroblastic proliferation in the submucosa. The tracheal wall showed congestion, edema, small-celled infiltration, and fibroblastic proliferation. The larger bronchi were filled with pus. Small diphtheritic areas were found on the mucosa, where the epithelium was entirely gone and the fibrinopurulent exudate was adherent. Walls of the bronchi were edematous, infiltrated with leucocytes, and the blood vessels were congested. Any epithelium remaining showed mucoid and hydropic degeneration. The lungs showed extreme congestion and numerous small hemorrhages. The alveoli for the greater part were overdistended, emphysematous, although there were many small atelectatic areas in the neighborhood of plugged bronchi. The atelectatic areas showed a marked edema. Practically all the bronchi and bronchioles were filled with a purulent exudate and around many there were areas of purulent bronchopneumonia. Colonies of cocci were found in the pus in the bronchi. Other organs showed intense congestion. No other organs showed specific changes with the exception of stomach and intestine, in which small sloughs were found, probably the result of local action of mustard gas swallowed in food or saliva.

This rabbit showed a severe purulent and diphtheritic inflammation of the upper respiratory tract and a purulent bronchopneumonia, due to a staphylococcus, secondary to the more severe lesions caused by the gassing.

SUMMARY OF EXPERIMENTAL WORK

From repeated and carefully controlled animal experiments the following conclusions were arrived at in regard to the production and nature of the respiratory lesions due to mustard gassing:

1. The respiratory lesions are proportionate to the concentration of mustard gas employed and to the length of exposure.

2. The mildest lesions are those produced by short exposures, such as ten to fifteen minutes, to dilutions of 1:110,000 or over; or very short exposures, one to several minutes, to higher concentrations.

3. Exposure to mustard gas causes almost immediate signs of nasal irritation on the part of the animal. It will almost immediately rub its nose and turn its back to the inflowing gas. Conjunctival symptoms, in the form of photophobia and increased lacrymation, usually appear within two to three hours, the respiratory symptoms developing two to three hours later, as a rule, in the form of snuffles, increased nasal secretion, or a more or less severe coryza. In the case of short exposure, or low concentration of the gas, the respiratory symptoms do not progress beyond a catarrhal stage.

4. In prolonged exposures, or exposures to higher concentrations, the respiratory symptoms appear at relatively the same time, but usually later than the conjunctivitis. They then increase in intensity for several days until a picture of diffuse diphtheritic inflammation of the respiratory tract is produced, as manifested by increasing difficulty in respiration, exudation, râles, and coughing. The animal may die within 48 hours, or later.

5. The pathologic lesions in the mildest cases consist of a superficial degeneration or necrosis of the epithelium of the mucous membrane, with congestion and edema and increased mucus secretion. These milder lesions are found chiefly in the anterior nares, the pharynx, larynx, and upper portion of trachea; but animals killed after such exposures invariably show a more or less marked pulmonary congestion and edema, increased bronchial secretion, and small, scattered atelectatic areas. From lesions of this degree recovery, without secondary infection, usually takes place.

6. The severer lesions consist of deeper necrosis of the mucosa of the respiratory tract and the formation of a diphtheritic membrane in the anterior nares, nasopharynx, larynx, trachea, and larger bronchi. The most severe lesions are always in the nares, pharynx, larynx, and upper part of the trachea, the intensity decreasing toward the bronchi. The respiratory columnar epithelium suffers more than the epithelium of the mouth cavity, although irregular areas of complete necrosis of the latter may be produced. The entire epithelium of the larynx, trachea, and larger bronchi may be killed outright and the surface covered with a diphtheritic membrane, which, for the greater part, is easily detached, forming a cast of the larynx, trachea, and larger bronchi. The laryngeal and tracheal walls show edema, congestion and small-celled infiltration, but the edema is always less marked than in the case of the subcutaneous tissues or the conjunctivæ.

7. In the severe cases, secondary infection with staphylococci almost invariably occurs, and the lesions in the larynx, trachea, and bronchi usually take on a purulent character within four to six days, if the animal lives that long.

8. In the mildest cases the lungs show congestion and edema with hydropic and mucoid degeneration of the epithelium of the bronchioles. In the more severe cases the necrosis of the epithelium extends into the smaller bronchial divisions and bronchioles and a secondary purulent bronchopneumonia, apparently usually due to staphylococci, follows. In these severer pulmonary lesions, atelectatic areas, due to the plugging of the bronchioles with exudate, usually alternate with emphysematous areas. The atelectatic areas are usually edematous or hemorrhagic. Secondary hemorrhage into the purulent bronchopneumonic areas is also frequent, in some cases the condition assuming the picture of a hemorrhagic bronchopneumonia. In the pneumonic areas following gassing, colonies of staphylococci are always present.

9. In the severe cases death may occur more quickly as the result of a diphtheritic or purulent laryngitis without the development of pneumonia, but in the majority of cases the cause of death, so far as the respiratory tract is concerned, is the development of an infective purulent bronchopneumonia secondary to the injury produced by the gassing.

10. Cases with localized diphtheritic necroses in nose, mouth, larynx, and trachea, without extensive bronchopneumonia, may recover with healing and cicatrization of these areas. Fibroblastic proliferation in such areas was noted as early as the fourth day after gassing. Cicatricial contractions of trachea or larynx may result from such healed lesions.

CLINICAL MATERIAL

The clinical features of mustard-gas lesions of the respiratory tract in man were studied in the cases of seven soldiers who were severely gassed in the manufacture of mustard gas, although wearing gas masks. The concentration of the gas to which these men were exposed was so strong that all received severe burns, two of the cases terminating fatally. In addition to these severe cases, data were secured from 63 other workers with mustard gas who had had at one time or another milder respiratory symptoms following accidental exposure to mustard-gas vapor.

CASE I.—Pvt. Ha. (Case 6, p. 549). Exposed one hour in two or three shifts. Within a few hours after the exposure he developed erythema of the skin, nausea, and vomiting and

complained of intense thirst. This patient developed no conjunctivitis, his eyes being sufficiently protected by the gas mask. Later, burns about the lips appeared, and within the next few days diphtheritic neeroses developed over the dorsum of tongue, uvula, hard and soft palate, pillars of fauces, tonsils, and pharynx. On the seventh day after the accident, large, moist râles were present over both lungs, and he was thought to have a diffuse bronchopneumonia. The patient died on the eleventh day after gassing. The autopsy report of his respiratory tract changes will be found below.

CASE 2.—Pvt. S. (Case 7, p. 549). Exposed three-quarters of an hour, in two or three shifts, to the same concentration as the preceding. During the next few hours, in addition to the development of conjunctivitis, nausea, and vomiting and erythema of the skin, he complained of intense thirst, and later showed patches of diphtheritic necrosis on the lips, angles of mouth, hard and soft palate, uvula, pillars, tonsils, buccal surfaces, dorsum of tongue, and gums. All of the mucous membrane of the mouth showed erythema and desquamation of the epithelium. When seen on the eighth day he could barely whisper and had physical signs of a diffuse bronchopneumonia. He died four weeks after the accident. Autopsy not permitted.

CASE 3.—Pvt. Mc. (Case 1, p. 544). Exposed 40 minutes in four shifts. Within a few hours after the exposure, coincidently with the nausea and vomiting and erythema of the skin, he complained of a very dry throat. For three days he had a hacking cough and complete aphonia. The roof of his mouth was very painful, and on the third day one of the sore places in his throat "seemed to burst" and he coughed up membranlike material, after which his symptoms were improved, but his voice remained husky and a bronchial cough persisted for some time. When examined eight days after the accident he had a catarrhal rhinitis and patches of diphtheritic necrosis over the mucous membrane of the mouth, particularly on the right pillar and in the posterior pharyngeal wall. Occasional loud, moist râles were heard over his thorax. Respirations increased.

CASE 4.—Pvt. W. (Case 5, p. 546). Exposed one-half to three-quarters of an hour in two or three shifts. In the first few hours after the exposure he developed mouth and throat symptoms in the form of a dry sore throat and could barely whisper. When examined eight days after the accident he showed diphtheritic necrosis of the mucous membrane of the lips, angles of the mouth, hard and soft palate, uvula, anterior and posterior pillars, tonsils, and posterior pharyngeal wall. The roof of the mouth was covered with a grayish-green diphtheritic membrane through which numerous discrete yellowish-white elevations appeared, suggesting small pustules on erythematous bases. On the eighth day he developed symptoms of a diffuse bronchopneumonia from which he later recovered, after, in the meantime, having expectorated a fibrinous bronchial cast, containing streptococci.

CASE 5.—Pvt. M. (Case 2, p. 544). Exposed one-half hour in one shift. Had severe thirst but no soreness of mouth or throat. He developed a temporary erythema of the mucosa of the hard palate, with a small patch of diphtheritic necrosis. Voice husky, frequent cough, and respiratory rate increased.

CASE 6.—Pvt. E. (Case 4, p. 546). Exposed 10 minutes in one exposure. On the next day complained of a very dry throat. He showed only a temporary erythema of the mucous membrane over the hard palate. When seen eight days later his voice was husky, and he had an occasional dry cough.

CASE 7.—Pvt. Hu. (Case 3, p. 546). Exposed 10 to 12 minutes in one shift. He developed a severe rhinitis and a sore throat, but showed only an erythema of the mucous membrane of the mouth. When seen eight days after the accident his voice was still husky, and he had a laryngeal cough.

A large number of other cases of mild respiratory lesions were also seen. All of these were in cases with conjunctivitis. These patients complained usually of a dry or sore throat, huskiness of voice, with or without an accompanying rhinitis. A dry laryngeal cough usually persisted for several days, a definite huskiness for a longer period. In two cases, short exposures to weak concentrations produced in susceptible individuals a fibrinopurulent rhinitis lasting several days. In the severe cases of mouth burns the most marked lesions were always on the hard and soft palate and the dorsum of the tongue. The mildest cases showed erythema of the same areas.

RESPIRATORY LESIONS AS SEEN AT AUTOPSY

CASE 1.—Pvt. Ha.

GROSS FINDINGS

Nose: Examination of anterior nares negative. No skin burns on nose.

Lips: No burns of mucosa of lips.

Mouth and neck organs: Tip of the tongue was negative. On the dorsum there were patches of grayish and grayish-white coating beneath which the mucous membrane was desquamated. When the coating was removed there was a denuded, reddened surface. These lesions increased in severity toward the root of the organ where they became diphtheritic in character and were covered with a greenish-gray membrane. (Fig. 201.) The tonsils and palatal arch showed areas of diphtheritic necrosis covered with a grayish membrane. Mucosa of the palate was markedly edematous and presented elevated, reddened and grayish areas. The tonsils were about normal in size, with deep crypts. The right was negative on section. The left tonsil showed membranous patches and, on section, crypts containing fibrinous exudate. Mucosa of pharynx was covered with a thick, grayish, tenacious membrane, which, when pulled off, left a denuded, reddened surface. The epiglottis was covered with a thick, grayish mucus and the glottis was filled with a similar mucus. Beneath this the mucosa was congested and showed small patches of superficial necrosis, but these lesions were less marked than in the pharynx. Below the glottis, the mucosa of the trachea was covered with a thick grayish mucus, beneath which the mucosa showed a congestion diminishing in intensity from above downward. There was no membrane in the trachea but in its lower portion and at the bifurcation there was a thick, grayish mucus in the lumen. The posterior wall of the trachea showed marked hypostasis but there was no visible necrosis of its mucosa. The esophagus showed congestion of its mucosa with superficial desquamation at the mouth but no changes below this.

Lungs: There was no fluid in either pleural cavity. The lungs met in the midline above the heart. Both lungs were free throughout. Pleural surfaces negative.

Left lung: There were delicate old adhesions between the upper and lower lobes. On the anterior surface of the lower lobe there was a small pigmented nodule beneath the pleura, a healed tubercle. There was no thickening or puckering of the pleura over the apex. Beneath the pleural surface there were numerous minute petechial hemorrhages which were largest and most abundant posteriorly. The lung was air-containing throughout. The upper lobe was voluminous and pink in color; the lower lobe showed marked hypostasis posteriorly. On section, the cut surface showed marked congestion and edema. Foamy fluid, thicker than the ordinary stasis edema, exuded abundantly from the cut surface. The lower lobe presented a marked hypostatic congestion. The small hemorrhages appeared soft and fresh and the blood showed no discoloration. Small fresh agonal lardaceous clots were found in the larger pulmonary vessels, but no thrombi or emboli were visible to the naked eye. No pneumonic areas, no abscesses, no hemorrhagic infarctions and no airless areas were found. Anthracosis was moderate. The main bronchi were filled with a thick, frothy fluid which was rather viscous and was grayish-white in color, but in the smaller branches became distinctly yellowish and thicker. Beneath this the mucosa of the bronchi was markedly congested.

Right lung: The right lung was very much heavier than the left and much deeper in color. There were delicate old adhesions between upper and middle and middle and lower lobes. The lower lobe posteriorly was almost black in color, the middle lobe deep red, while the upper lobe was more pinkish. The subpleural hemorrhages were more marked in this lung than on the left side. The anterior margins of the lobes showed emphysema. The greater part of the lower lobe showed a partial atelectasis and posteriorly a firm airless area almost black in color, about the size of a hen's egg. On section, there was extreme congestion and edema, with areas of atelectasis throughout the lower lobe. Throughout the entire lung there were numerous firm, elevated, airless areas of small size, that were not wedge-shaped. The large airless area in the lower lobe was wedge-shaped, with its base toward the surface, deep red, almost black in color, and showed in its center a softer, lighter area, apparently around the blood vessel. No thrombi or emboli could be seen with the naked eye. The bronchi showed the same fluid content and changes in the mucosa as on the left.

Bronchial nodes: The bronchial nodes on both sides were rather small, soft, edematous and but slightly pigmented.



FIG. 201.—Mouth and neck organs of fatal human case. Mustard-gas lesions of tongue, pharynx, larynx, and trachea. Dorsum of tongue shows diphtheritic eschar. Diphtheritic necrosis of pharynx, mucosa of larynx, and trachea. Marked edema with diphtheritic necrosis of the arytenoepiglottidean fold

MICROSCOPIC FINDINGS

Mouth: Sections from the dorsum of the tongue showed patches of diphtheritic necrosis and small ulcers from which the membrane had been loosened. The submucosa showed intense congestion, small-celled infiltration, some fibroblastic proliferation and numerous capillary thromboses. Some of the dilated vessels, either capillaries or lymphatics, were filled with coarse threads of fibrin without red blood-cells and with only an occasional leucocyte. The mucous glands showed intense mucoid degeneration with small-celled infiltration and many of the ducts were dilated and filled with mucus. Regeneration of the epithelium from the deepest portions of the folds and mouths of the mucous glands had begun. (Fig. 202.)

Pharynx: Sections of the pharyngeal wall showed intact epithelium covered with a thick mucus. The submucosa showed marked congestion, edema, and polynuclear infiltration, with small areas of hemorrhage. There were numerous dilated capillaries or lymphatics filled



FIG. 202.—Case I, Private Ha. Mustard-gas lesion of dorsum of tongue. Base of ulcer from which the diphtheritic membrane has become detached

with coarse threads of fibrin without red blood cells or leucocytes. The mucous glands showed marked mucoid degeneration. The tonsils showed marked congestion and edema. The greater part of the epithelium was intact, but there were localized patches of diphtheritic necrosis. There was an increase of the stroma and many sclerotic vessels.

Larynx: Sections from larynx showed a desquamative catarrhal laryngitis with small areas of diphtheritis. (Fig. 203.) The epithelium was for the greater part necrotic, either entirely gone or represented by a single layer of nuclei. On the surface there was a thick mucofibrinous exudate forming a cast of the entire lumen and for the greater part separated from the necrotic surface. The submucosa showed congestion, edema and slight leucocyte infiltration.

Trachea: The trachea presented the same condition as the larynx, a desquamative necrotic tracheitis with the formation of a thin mucofibrinous membrane over the surface.

Bronchi: The larger bronchi were filled with a thick mucous exudate containing many desquamated cells, some polynuclear leucocytes and a few red blood cells, with little or no

fibrin. The epithelium of the mucosa was in part intact, showing hydropic or mucoid degeneration, and in part desquamated. The bronchial walls showed intense engorgement of the vessels, well-marked edema and a moderate small-celled infiltration. The mucous glands showed marked mucoid degeneration. The picture was that of a catarrhal desquamative bronchitis. (Fig. 204.)

Lungs: The lungs showed extreme congestion and edema, with numerous minute hemorrhages by diapedesis. Areas of emphysema and atelectasis alternated throughout the lung. The atelectatic areas showed the most marked edema and were usually the areas in which hemorrhages were found. No pneumonic areas were found. The airless area in the lower right lobe was a recent hemorrhagic infarct, the central lighter portion being an artery obturated by a recent mixed thrombus. Other smaller recent hemorrhagic infarcts were found beneath the pleura of the right lung, with recent thrombi in the vessels leading to these areas. All the smaller bronchi and bronchioles were dilated and filled with a seromu-

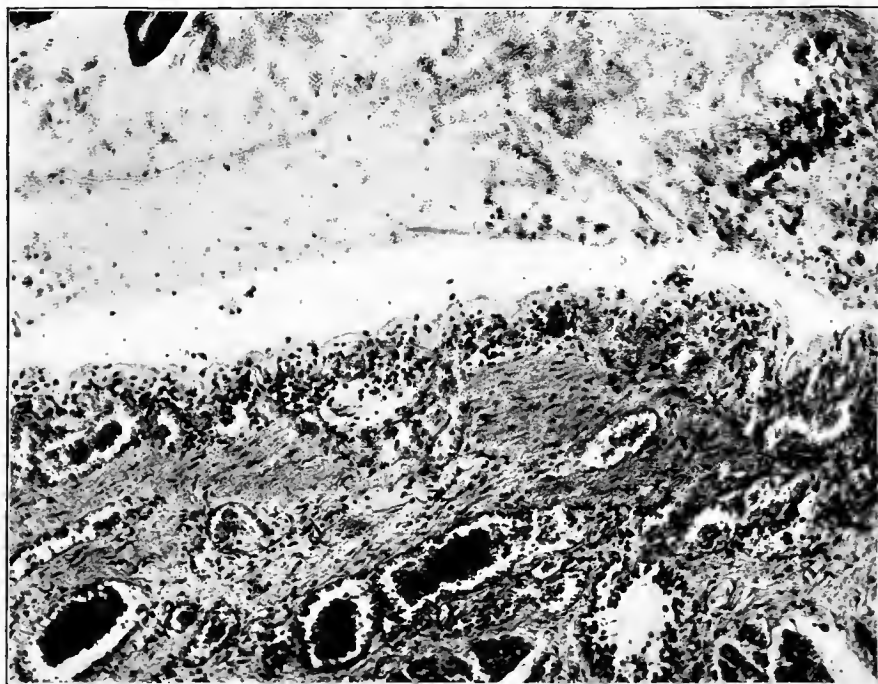


FIG. 203.—Case I, Private IIa. Section of diphtheritic lesion on vocal cord. Epithelium of mucosa completely destroyed and a mucofibrinous membrane partly detached from the surface. Extreme hyperemia of the vessels. Some small-celled infiltration

oid fluid containing desquamated cells with some fibrin and occasional red cells. The epithelium of the smaller bronchi was intact for the greater part, but showed marked mucoid or hydropic degeneration. In many bronchioles desquamation of the epithelium had taken place. In no bronchi or bronchioles was there any purulent exudate. There were no old thrombi or emboli, and fat stains of frozen sections showed no fat emboli. Smears of the bronchial exudate and from the cut surface of the lung showed only occasional diplococci.

This case presented a marked degree of mustard-gas degeneration and necrosis of the epithelium of the mouth cavity, larynx and trachea, decreasing in intensity to the larger bronchi and bronchial subdivisions, without infection or pneumonia. Death, in this case, probably resulted from shock and toxemia from the extensive areas of necrosed skin and secondary infection.

SUMMARY OF CLINICAL OBSERVATIONS

From the clinical cases coming under observation, mustard-gas lesions of the respiratory tract in man were of the same nature as those produced experimentally in animals. In the milder cases there was an injury to the epithelium of the mucosa of the upper respiratory tract, particularly of the anterior nares, hard and soft palate, dorsum of tongue, pharynx, larynx, and upper part of trachea. Rhinitis and laryngeal huskiness and cough, with sore throat and thirst, were the most common symptoms in individuals exposed to light and moderate concentrations. From these conditions recovery was usually prompt, but laryngeal huskiness and irritation might continue for some days or even weeks. No instance of secondary infection was observed in such cases.

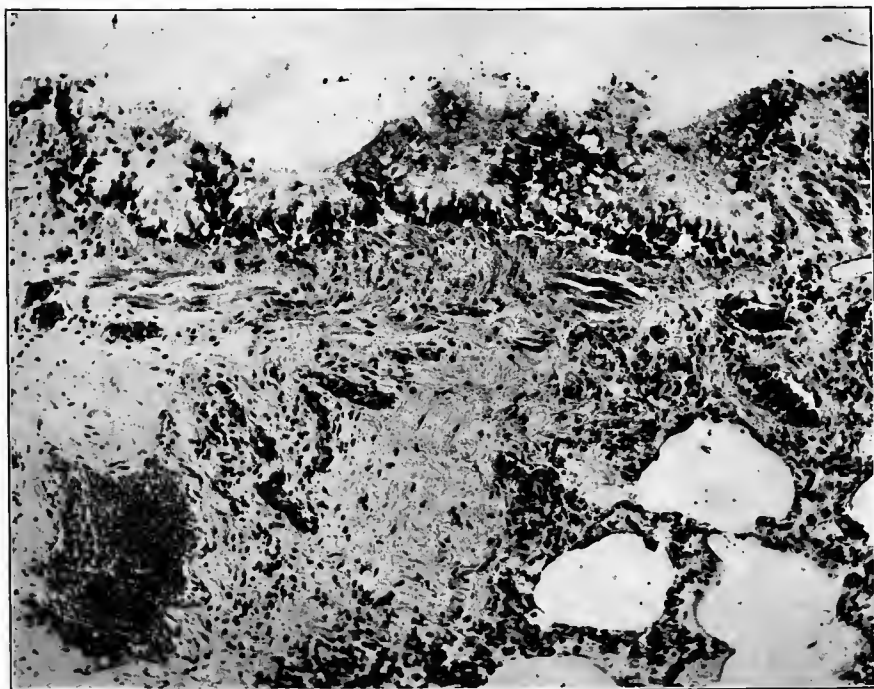


FIG. 204.—Case 1, Private Ha. Section of main division of bronchus. Picture of catarrhal bronchitis. Marked mucoid degeneration and vacuolation of the bronchial epithelium. Congestion, small-celled infiltration and edema of the bronchial wall

In the more severe human cases, there was a greater degree of degeneration and necrosis of the epithelium of the respiratory tract, extending into the bronchi, but diminishing from the upper part of the trachea down, the most severe lesions being eschars on the palate, dorsum of tongue, pharynx and larynx.

Associated with these was a widespread catarrhal tracheitis and bronchitis, with congestion and edema of the lungs. The one case autopsied showed no pneumonia. Under the conditions of warfare more severe exposures to mustard gas may produce diphtheritic lesions of larynx, trachea, and bronchi, terminating in bronchopneumonia.

CONCLUSIONS

1. The action of dichlorethylsulphide (mustard gas) upon the epithelium of the respiratory tract is escharotic in character, similar to its action upon the epidermis, cornea, and conjunctival epithelium. Degeneration or complete necrosis of the epithelium, or deeper necrosis extending into the submucosa constitute the primary lesions produced in the respiratory tract by mustard gas in weak or strong concentrations. These lesions are most marked in the anterior nares, mouth, pharynx, larynx, and upper part of trachea, diminishing in intensity toward the lungs. In the more severe cases, however, the bronchial epithelium may also undergo degeneration or necrosis. The subepithelial edema in the upper respiratory tract is not at all comparable in degree to that associated with mustard-gas lesions of the skin and conjunctiva.

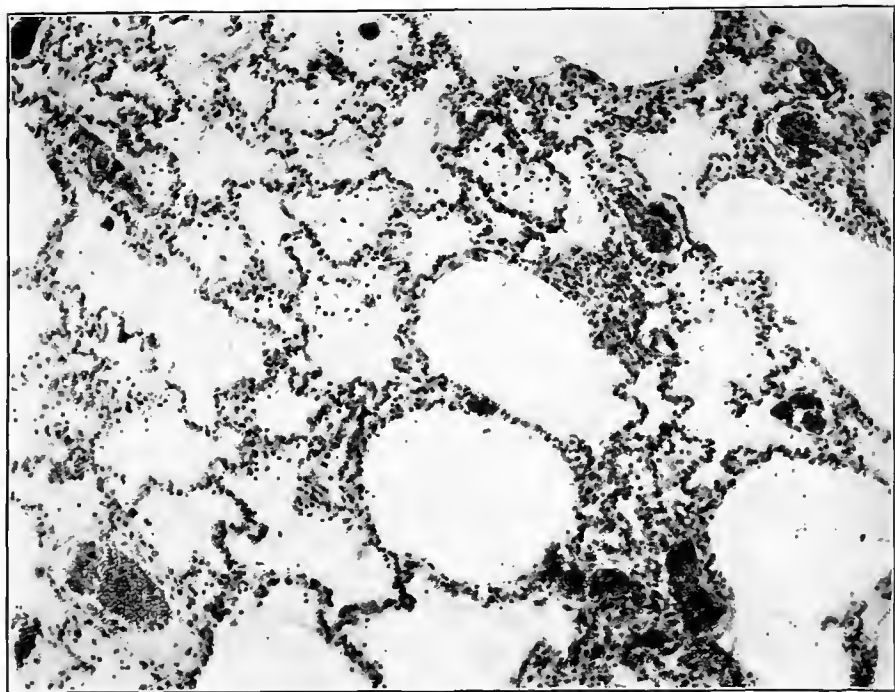


FIG. 205.—Case I, Private Ila. Section of upper lobe of lung. Congestion and edema. Acute emphysema

2. Following the primary lesion there develops a catarrhal or a diphtheritic rhinitis, localized stomatitis, pharyngitis, laryngitis, tracheitis, or bronchitis. Cicatricial contractions or sclerosis may result from the healing of such lesions.

3. In even the mildest cases there is marked congestion and edema of the lungs, catarrhal bronchitis, and localized atelectasis due to bronchial plugging. In the more severe cases the bronchitis may be diphtheritic in character. Secondary infection may occur, and, following the development of a purulent bronchitis, a purulent bronchopneumonia may result. We have observed no pneumonia resulting directly from the gassing. All of the pneumonias observed, following the gassing, have been the result of secondary infection.

GASTROINTESTINAL LESIONS^c

BY FEEDING

Capsules containing 0.06 to 0.24 c. c. of dichlorethylsulphide were given to rabbits and guinea pigs in olive oil, butter, and lard; similar capsules were given in meat to dogs. Animals were kept fasting, but were given water to drink. They were killed in series to get the complete pathologic picture from beginning to end of the process. For the purpose of brevity protocols are omitted, and the results of the experimental work are condensed as follows:

SYMPTOMS

The symptoms, which appeared, usually in from 1 to 2 hours, were vomiting; irritation of mucous membranes of mouth; profuse salivation; ultimately foul

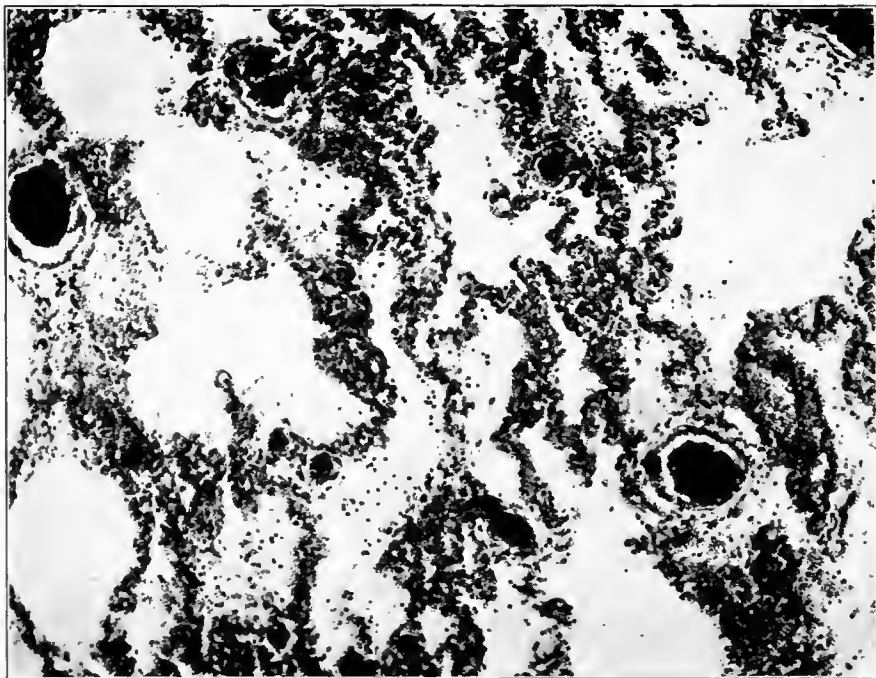


FIG. 206.—Case 1, Private Ha. Section of lower lobe of lung. More intense congestion. Minute hemorrhages by diapedesis. Area of partial atelectasis, alternating with emphysematous areas. Edema

discharge from nose and mouth; foul diarrhea, at times tarry stools; depression; refusal of food and water. When the animal was allowed to live there was progressive anorexia, and weakness; by the sixth day it was so weak that it lay prostrate. Animals became greatly emaciated, with odor of foul putrefaction. Foul discharge from mouth. Death occurred usually by the twelfth day, from 0.03 to 0.06 c. c. doses, within three to five days from the 0.24 c. c. dose, for dogs; sooner for guinea pigs and rabbits.

GROSS PATHOLOGY

Delayed rigor mortis in animals not immediately autopsied. Emaciation. No free gas or fluid in peritoneal cavity. No general peritonitis. Liver con-

^c For the gastrointestinal lesions produced by subcutaneous and intravenous injections of mustard gas the reader is referred to general pathology, p. 632.

gested; gall-bladder dilated; spleen anemic, small and dry. Heart showed dilatation of right side. Peculiar chicken-fat clots in right ventricle of dogs. Lungs showed varying degrees of congestion; no pneumonia. Kidneys congested. Stomach and duodenum distended with gas and containing greenish or black fluid. Mucous membrane showed varying degrees of necrosis, localized in patches or extending over the entire surface. The necrosed areas appeared greenish-brown or gray, to black, without much inflammatory reaction. In the milder cases the mucosa at times showed marked congestion. Very little hemorrhage in stomach. Necrotic areas were usually thinned, but the animal died before perforation occurred. Early peritonitis, over the thinned areas, occurred. Self-digestion by the stomach juices of the necrotic surface was delayed, from the inhibition of stomach secretions. Clean ulcers were not seen in the early cases, but were found in from 6 to 12 days, the ulcer extending into the muscle coat. The stomach lesions did not show the characteristic edema produced by dichlorethylsulphide in the skin and conjunctiva. A moderate edema was observed only in the cardiac end. The nonhemorrhagic character of the gastric lesions was also striking. Throughout the intestines there were patches of necrosis with congestion and slight hemorrhage, and more or less marked catarrh. Mesenteric glands swollen, edematous and congested. In the mouth, nose, pharynx, and esophagus of a certain proportion of the animals marked necrotic lesions, with secondary infection, occurred as the result of local contact with the gas in swallowing or vomiting.

MICROSCOPIC PATHOLOGY

Gastrointestinal mucosa showed varying stages and degrees of necrosis, involving the upper layers of the mucosa or extending through the submucosa into the muscle coats. In no case did the ulcer extend through the muscle. Preserved portions of the mucosa showed dilated glands filled with granular or thready precipitate, or colloid masses, resembling hyaline casts. The epithelium of the deeper portions of the glands often showed a marked hydropic degeneration or liquefaction necrosis. There was usually little or no edema of the submucosa or tissues of the neighboring stomach wall. The eschar might be adherent to the surface or the floor of the ulcer might consist of the muscle coats. These showed polynuclear infiltration, congestion, some fibrinous exudate into the tissues, and occasionally hemorrhage. In the older cases there was often a marked small-celled infiltration of the muscle coats, extending to the subserosa, with fibroblastic proliferation of the latter and beginning peritonitis. The necrotic areas in the intestine were similar but showed a more marked leucocyte infiltration, often extending to the serosa, but without any overlying peritonitis. The necrosis of the mucosa was most marked over the lymphoid tissue, Peyer's patches often being nearly completely necrosed. Numerous putrefactive bacteria were found in the necrotic areas of the mucosa. The entire mucosa was congested and inflamed, showing occasional hemorrhages. The inflamed mucosa was but moderately edematous. There was marked mucoid degeneration of the epithelium. The mesentery was edematous and showed at the insertion areas of inflammation. The mesenteric glands showed sinus catarrh and were congested. (Figs. 207, 208.)

BY INHALATION

In animals gassed in the gassing chamber and not dying within several days there were found practically always a more or less severe congestion and catarrhal inflammation, which were more severe in the small intestine than in the stomach. In some cases more severe lesions were found in the upper part of the digestive tract (diphtheritic necrosis, catarrhal inflammation, ulceration, etc.), but these could be explained as the result of gas swallowed with the air, saliva, or with food, and must be interpreted as direct local lesions. (Fig. 209.) The generalized catarrhal condition of the small intestine may be explained by the assumption that dichlorethylsulphide, or some substance resulting from it, is excreted by the intestine or through the bile, or by the direct local action of minute quantities of mustard gas taken in with food or saliva and diffused throughout the gastrointestinal contents.

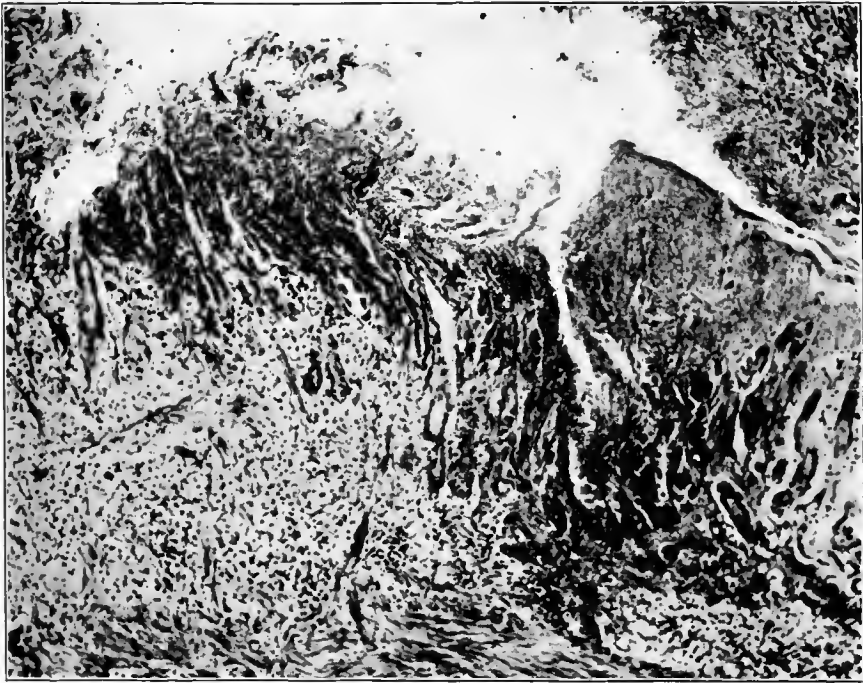


FIG. 207.—Dog. Received four minimis of dichlorethylsulphide on meat. Died five days afterwards. Small mustard-gas eschar in stomach mucosa. Early fibroblastic proliferation

CLINICAL OBSERVATIONS

In the severe cases of mustard gassing observed, marked nausea and vomiting, gastrointestinal pain, and diarrhea either preceded or were synchronous with the development of the cutaneous burns. These symptoms were reflex in nature and may be regarded as symptoms of the severe shock from which the patients suffered at that time. The gastrointestinal symptoms seen in several patients after the symptoms of severe shock had disappeared were reflex and dependent upon the laryngotracheal-bronchial irritation (coughing).

In the fatal case the following gross appearances in the gastrointestinal tract were noted.

The stomach contained a small amount of thin, grayish fluid, slightly blood stained, and some milk curds. Throughout the entire mucosa there were numerous small petechial hemorrhages, these being most numerous toward the cardia, where the mucosa was sprinkled with them, many of them being confluent. They all appeared very fresh, the blood not being discolored and having no erosions or ulcerations over them. The gastric mucosa was thin, smooth, and soft, with early post-mortem change. The duodenum contained a thin, grayish bile-stained fluid, the mucosa was congested and covered with a tenacious, thick, grayish mucus. Just below the pylorus there were numerous hemorrhages in the mucosa. The small intestine was distended with gas, and at intervals there were small collections of thin fecal matter slightly bile stained. The mucosa was congested, and there was marked

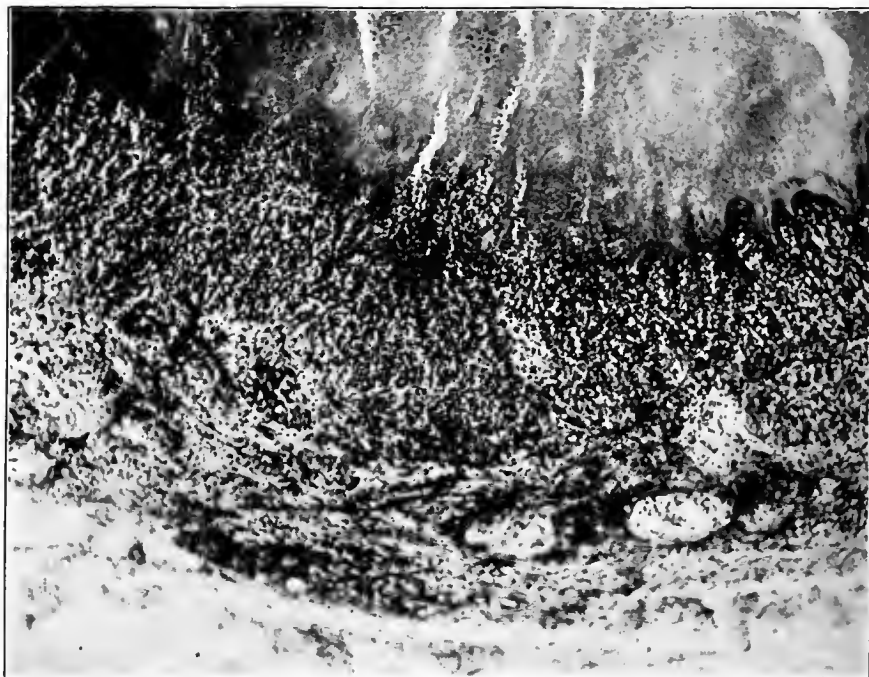


FIG. 208.—Dog. Received 0.06 c. c. of dichlorethylsulphide in capsule. Died 12 days later. Portion of base of very large eschar of stomach wall, extending nearly to the serosa. Marked leucocyte infiltration

hypostasis in portions of the loops without other changes. The colon contained gas, and some formed fecal masses. The mucosa was negative.

Microscopic findings.—The stomach showed a marked congestion of the vessels of the mucosa, with numerous fresh hemorrhages. Post-mortem digestion of the upper portion of the mucosa. The duodenum showed a post-mortem desquamation of the surface epithelium, slight catarrh of the glands, and congestion and edema of the mucosa. Colon showed a similar condition. Appendix showed evidences of old inflammation. No active process. The mesenteric glands showed a marked sinus catarrh, with many hemophages present in the sinuses.

It was hardly probable that the gastrointestinal changes observed in this case were the direct result of the mustard gassing. It is much more likely that they were entirely secondary phenomena.

CONCLUSIONS

1. Direct application of mustard gas to the mucosa of stomach or intestine by means of contaminated food produced localized degeneration, necrosis, and ulceration similar in type to the lesions of the respiratory tract.

2. The mild catarrhal conditions and small localized eschars of the stomach and upper portion of the small intestine seen in animals gassed in the gassing chamber may be explained as the result of minute quantities of mustard gas swallowed with air or dissolved in the saliva.

3. The gastrointestinal symptoms seen in gassed human beings are probably chiefly reflex, associated either with shock or with the respiratory irritation. As in other forms of gassing, it is probable that erosions or ulcers of



FIG. 209.—Rabbit. Exposed 12 hours to a concentration of 1 to 50,000. Died 92 hours after gassing. Mustard-gas eschar on tongue

the stomach and intestine may be embolic in character, the emboli arising in the primary or infected mustard-gas lesions of the skin or elsewhere. It is also possible that in man, as in the case of animals, localized eschars of the gastrointestinal mucosa may be produced by the direct action of mustard gas swallowed in contaminated food or saliva.

GENERAL PATHOLOGY OF ANIMALS GIVEN LOCAL APPLICATIONS OF DICHLORETHYLSULPHIDE TO SKIN OR CONJUNCTIVA, OR EXPOSED TO ITS VAPOR IN GASSING CHAMBER

From observations made upon a large number of animals exposed to mustard gas, either by direct applications to the skin or eyes, or in the gassing chamber, the systemic symptoms shown consisted of gastrointestinal disturb-

ances, such as vomiting and diarrhea; disturbance of heart rate, usually an increased rate, but in severe cases the rate may be slowed; lowering of the temperature except with infection; decreased urinary elimination; in the blood a secondary anemia, with or without leucocytosis; and nervous symptoms, as increased reflex excitability, tremors, and convulsions, or marked depression, stupor, and coma. The great majority of slightly or moderately gassed animals showed no systemic phenomena. The most constant of the general symptoms were the gastrointestinal. While a certain number of cases showing these symptoms could be explained as resulting from slight quantities of mustard gas swallowed in the air or saliva, or on food particles, it is probable that the gastrointestinal symptoms were chiefly reflex to the respiratory irritation, or were a part of the general phenomena of shock. In all severe dichlorethylsulphide gassing an initial shock was very common, and the changes in temperature, circulation, etc., formed part of the clinical picture of this condition. With the development of pneumonia or localized infection the usual symptoms attending such processes were observable.

Nothing was seen that corroborated Victor Meyer's idea that the toxic action of mustard gas is exerted chiefly through the blood; indeed, all observations made one certain that local applications of mustard gas to the skin of distant parts can not produce conjunctivitis or local lesions at other sites.

In rabbits gassed in the gassing chamber at varying concentrations there occurred within 24 hours following the gassing a distinct concentration of the blood, as shown by a polycythemia varying from one to two millions increase, and an increase in the leucocytes. This concentration might last for several days, after which the number of red blood cells slowly came down to normal. With the advent of secondary infection, which might take place at any time from the second to seventh day after gassing, there was a leucocytosis which might reach 50,000. If the animal lived and showed increasing cachexia as the result of infection, the blood picture of a secondary anemia developed. This, however, had no direct relationship to the toxic action of dichlorethylsulphide. These investigations, therefore, confirmed the previous observations made in this laboratory that cutaneous, ocular or respiratory gassing with dichlorethylsulphide had no direct action upon the blood or bone marrow.

Four selected protocols illustrating these points are given:

RABBIT 90.—Gassed six hours at a concentration of 1 to 20,000:

	Red count	White count
June 20.....	4, 710, 000	7, 400
June 21.....	5, 470, 000	16, 000
June 22.....	5, 290, 000	9, 200
June 23.....	5, 130, 000	17, 400
June 24.....	5, 000, 000	18, 400
June 25.....	5, 130, 000	13, 200
Gassed from 2.45 p. m. to 8.45 p. m., June 27.		
June 28:		
8 a. m.....	6, 560, 000	15, 700
2 p. m.....	7, 800, 000	13, 600
June 29.....	5, 510, 000	49, 600
June 30.....	4, 970, 000	14, 400
July 1.....	6, 460, 000	31, 600
July 2.....	5, 270, 000	15, 800
July 3.....	4, 180, 000	18, 000

	Differential counts			
	Before gassing		After gassing	
	June 21	June 25	June 28	July 3
	<i>Per cent</i>	<i>Per cent</i>	<i>Per cent</i>	<i>Per cent</i>
Lymphocytes.....	36	28	27	15
Large mononuclears.....	7	3	1.5	1
Polynuclears.....	52	66	70	81
Eosinophiles.....	4	2	.5	3
Mast cells.....	1	1	1

RABBIT 91.—Gassed six hours at a concentration of 1 to 20,000:

	Red count	White count
June 20.....	5,860,000	14,000
June 21.....	5,720,000	14,000
June 22.....	6,000,000	12,800
June 23.....	5,560,000	11,400
June 24.....	5,070,000	17,600
June 25.....	5,890,000	10,800
Gassed from 2.45 p. m. to 8.45 p. m., June 27.		
June 28:		
8 a. m.....	7,400,000	34,800
2 p. m.....	7,080,000	16,000
Died night of June 28-29.		

	Differential counts	
	Before gassing	After gassing
	June 20	June 28
	<i>Per cent</i>	<i>Per cent</i>
Lymphocytes.....	25	14
Large mononuclears.....	3	2
Polynuclears.....	69	82
Eosinophiles.....	3	2
Mast cells.....

RABBIT 92.—Gassed one hour at a concentration of 1 to 30,000:

	Red count	White count
June 20.....	5,200,000	10,200
June 21.....	4,900,000	17,600
June 22.....	4,720,000	13,600
June 23.....	4,900,000	14,400
June 24.....	5,120,000	15,200
June 25.....	5,650,000	10,800
Gassed from 10 a. m. to 11 a. m. on June 28.		
June 29.....	6,800,000	12,000
June 30.....	5,290,000	14,200
July 1.....	5,100,000	22,200
July 2.....	5,020,000	15,700
Died during night of July 1-2.		

	Differential counts		
	Before gassing	After gassing	
	June 25	June 29	July 2
	<i>Per cent</i>	<i>Per cent</i>	<i>Per cent</i>
Lymphocytes.....	39	16	16
Large mononuclears.....	2	9
Polynuclears.....	53	73	84
Eosinophiles.....	6	2
Mast cells.....

RABBIT 93.—Gassed one hour at 1 to 30,000:

	Red count	White count
June 20.....	6, 100, 000	10, 000
June 21.....	6, 200, 000	9, 400
June 22.....	5, 730, 000	9, 200
June 23.....	5, 590, 000	8, 600
June 24.....	5, 840, 000	10, 000
June 25.....	5, 700, 000	8, 200
Gassed from 10 a. m. to 11 a. m. June 28.		
June 29.....	6, 250, 000	28, 000
June 30.....	6, 360, 000	11, 500
July 1.....	5, 100, 000	12, 200
July 2.....	5, 640, 000	10, 500
July 3.....	6, 050, 000	9, 200

	Differential counts	
	Before gassing	After gassing
	June 25	July 3
	Per cent	Per cent
Lymphocytes.....	32	28
Large mononuclears.....	2	2
Polynuclears.....	60	70
Eosinophiles.....	4	
Mast cells.....	2	

Likewise, the pathologic findings in gassed animals gave no convincing evidence of the absorption of mustard gas into the blood from the skin, eyes, or respiratory tract. The general pathology was as follows:

Central nervous system.—Congestion; very rarely minute hemorrhages; in infected cases emboli were seen rarely.

Thyroid.—Congestion; no other changes, except as involved directly from the laryngeal lesions. This event was common enough in the severe cases of laryngeal and tracheal diphtheritis, when the thyroid was congested, edematous and infiltrated with leucocytes.

Heart.—Ventricles usually dilated. No changes observable in heart muscle.

Aorta.—Intima of great vessels occasionally showed fatty streaks.

Lung.—When not involved directly through the respiratory tract, as in local application to the skin, the lung showed congestion, with or without edema. In the case of infected skin or eye lesions pulmonary emboli and metastatic pneumonia may occur.

Spleen.—Congested. In some cases an increase in the number of pigmented phagocytes.

Adrenals.—Congestion. Occasionally minute hemorrhages in medulla. (These were probably post-mortem.)

Kidneys.—Congestion. Frequently slight cloudy swelling. In infected cases more marked cloudy swelling, casts.

Pancreas.—Congestion.

Liver.—Marked congestion. In the majority of cases liver cells were normal; slight cloudy swelling and fatty changes were not rare, but their occurrence did not suggest any direct relationship with the gassing.

Gall-bladder.—A thinner, watery bile was usually present.

Gastrointestinal tract.—Congestion and mucous catarrh were always present. Minute hemorrhages and erosions were frequently seen in stomach

(vomiting?). Very rarely embolic hemorrhages and erosions occurred, especially in animals with large eschars, or infected lesions. At times local eschars of the gastric mucosa occurred; these were explainable as due to ingestion of contaminated food or saliva. The marked salivation seen in many animals and the swallowing of quantities of such saliva containing small amounts of mustard gas, offered a plausible explanation for the catarrhal conditions found in the gastrointestinal tract, without assuming, as some writers have done, that they were due to an excretion of mustard gas through the gastrointestinal mucosa. The intense splanchnic congestion usually present might also serve to explain the gastrointestinal conditions.

Mesenteric lymph nodes.—Congestion and edema.

Genital organs.—No changes noted.

Urinary bladder.—Negative.

CLINICAL PATHOLOGY OF HUMAN CASES

The clinical pathology of a series of thirty cases gassed by exposure to mustard-gas vapors was studied.^f Nine of these cases were very severe, two resulting fatally. The others presented lesser grades of severity from a mild conjunctivitis only to severe skin burns. Unfortunately the study of the severe cases could not be begun until the tenth day after gassing, and observations as to the clinical pathology of these cases must be correspondingly modified. The results of this study are summed up in the following:

1. Mild cases of mustard-gas burns of the skin showed no changes in the blood or urine.
2. Moderately severe and severe cases of mustard-gas burns of the skin with some involvement of the upper respiratory tract showed after the first week definite changes in urine, blood urea, and blood.
3. The urinary changes consisted in a diminution of the urinary output, increased concentration and acidity, albuminuria, and diminished urea and chloride output. In the sediment there might be found casts, renal epithelium, red blood cells, and an increased number of leucocytes. Under forced fluids prompt improvement occurred.
4. Coincident with these urinary changes the blood urea was found to be high, but approached normal with the improvement in the urinary condition when fluids were forced.
5. The blood showed a slight secondary anemia, with a well-marked polymorphonuclear leucocytosis, a definite eosinophilia, and the appearance of myelocytes and young forms of leucocytes.^g The blood platelets were usually

^f By Dr. George R. Hermann.

^g Krumphaar (Rôle of the Blood and the Bone Marrow in Certain Forms of Gas Poisoning. *Journal of the American Medical Association*, 1919, lxxii, No. 1,139) discussing the hematologic examinations made in a series of patients gassed with mustard gas, concluded that there is an initial leucocytosis followed by a more or less extreme degree of leucopenia, which persists even in the presence of bronchopneumonia, and is very probably an important contributing factor to the high mortality of severe cases. Should the leucocyte count fall below 1,000 per c. mm. a "myelocyte crisis" may bring about a partial amelioration; but in the two cases of this kind observed, this did not serve to protect them from a fatal outcome. Lessened blood formation is also indicated by the production of anemia without blast-cell formation and diminution in the number of blood platelets. In the earlier stages the coagulation time is decreased, and in the later stages of severe cases it is increased.

In the observations recorded in this chapter experience with human cases of mustard-gas poisoning, even the fatal cases, and with experimental animal gassing gave results in contradiction to those obtained by Krumphaar. Leucopenia was never observed; on the contrary, there was a definite leucocytosis in all severe and moderately severe cases, with a mild secondary anemia, and an increase in the blood platelets instead of a decrease. There was also very frequently an increase in the eosinophiles.

increased. No evidence of hemolysis was found. These changes indicated a disturbance in the white cell formation rather than in the red blood cell group. No leucopenia was noted at any time. The leucocytosis reached its height coincidentally with the height of the secondary infection and fell with the improvement of the infection.

6. The temperature, pulse, and respiration charts showed in the severe cases an initial period of shock. With the development of the necrosis and the secondary infection there was a corresponding febrile reaction.

7. The bacteriologic examination of the infected skin lesions and furuncles showed constantly the presence of staphylococcus pyogenes aureus. In the one bronchial cast obtained streptococci were present.

8. We believe that the changes in the blood and urine may be interpreted as dependent upon the secondary infection and, in part, possibly, to the absorption of toxic products from the necrotic skin, rather than to any direct toxic action of mustard gas.

GENERAL TOXIC ACTION

No evidences of a toxic action upon the internal organs were seen in any of the lesions of mustard gas produced by direct application or by exposure to its vapor. Clinical studies, as far as carried out, showed increased blood urea, decreased urea and chloride output, decreased quantitative urinary output, and increased specific gravity, with increased acidity. The toxic symptoms observed could be explained as the result of the skin destruction, damage to the respiratory tract, secondary infection, decubitus, with resulting absorption, etc. In the earlier stages symptoms of severe shock might be present.

SEQUELAE

After healing of the skin lesions a severe itching might persist for many weeks or months. This was true, even of the mildest lesions; accompanying the itching the affected part might show a branny desquamation, or secondary vesicles might develop after rubbing (Nikolsky's sign).

AUTOPSY

The protocol of the gross and microscopic general pathology of the one human autopsy case of fatal poisoning from mustard gas is given in full, with the exception of the respiratory and gastrointestinal tracts, which have already been quoted (pp. 611, 620).

PROTOCOL

(Autopsy by Dr. A. S. Warthin, 2 p. m., July 8, 1918.)

Pvt. Ha. Died, 12.30 a. m., July 8, 1918.

External examination.—Young adult male body; length 170 cm.; strong build, frame large, thorax deep, epigastric angle a right angle, abdomen on level with ribs. Musculature good, well developed. Panniculus abundant, particularly over abdomen and thighs. Hips rounded, slightly of feminine type. Neck thick, thyroid small, facies slightly suggestive of mouth breathing; general appearances of body suggest the lymphatic constitution. All regional lymph nodes prominent. Hair of head abundant, dull brownish in color, dry; scalp shows much dandruff. Face shaven, beard not heavy, body hair fairly abundant; pubic hair of feminine type. External genitals small, serotum small, tight; testicles small; penis medium size, moderate phimosis. No anomalies. No deformities, defects, or mutilations. No surgical wounds or scars.

Hypostasis.—Moderate post-mortem hypostasis, pale in color, except over hyperemic areas. Superficial veins on upper portion of body contain but little blood.

Rigor mortis.—Marked rigor mortis throughout body, except in right arm, where it has been broken by manipulation of the arm.

Body heat.—Body is cold. (Cooled by undertaker.)

Odor.—Marked odor of gangrene over the skin, particularly from that of back.

Skin.—Marked pigmentation of skin of face, hands, and forearms. Right hand shows irregular patches of pigmentation alternating with paler recent scars of older (mustard gas) burns. Hands show irregular patches, particularly between the fingers, of desquamation of the horny layer. No recent burns on hands.

Over the greater part of the body, from the collar line down to the boot line, the skin presents the appearance of a chemical burn, varying in degree from hyperemia, slight desquamation, dried blebs and bullæ, denuded areas, to areas of well-marked necrosis and eschar formation. These lesions are most severe in the axillary regions, inner aspect of arms, bends of elbows, flanks, genitals, thighs, and back. Severe lesions completely encircle both thighs, and are particularly marked posteriorly where there is extreme necrosis, secondary infection, and pus formation. The necrosis is very marked over the entire back, neck, shoulders, and buttocks, where the skin is discolored, mottled red, grayish, yellowish-gray, brown, black, or greenish, with marked gangrenous odor. Deeper points of hyperemia corresponding to the hair follicles show in these discolored areas. Over a large part of these lesions the epidermis is desquamated in large bullæ, and the desquamated surface is brown, yellow, or red. There are no large hemorrhages into these lesions, and very few petechial hemorrhages, the reddened areas being hyperemic only, the redness disappearing on pressure. From the discolored moist areas a cloudy foul-smelling serum exudes. This is not blood stained in any region. Through the hyperemic areas in many regions the hair follicles appear as opaque, yellowish miliary nodules. These are particularly marked over the scrotum.

The skin of the abdomen is hyperemic, with a pale belted line corresponding to the protection afforded by belt worn by patient. This belted area of less injury disappears in the flanks and shows but slightly on the back. The anterior surfaces of the thighs are bright scarlet; marked hyperemia. The hyperemia stops rather abruptly over the legs about 15 cm. below the lower border of the patella. The lower portions of the legs show practically no involvement anteriorly; posteriorly there is slight discoloration and hyperemia (hypostasis?). The feet show no lesions.

The face shows no lesions except on the right side, around and below the right ear, where there is a slight desquamation of the epidermis, with some reddening of the edges and elevated portions of the lobe of the ear. Below the left ear there is slight desquamation without reddening. Over the neck, below the chin, are patches of dried vesicles, brownish red where the epidermis is desquamated, and red where it is still intact. The hair shows no changes. On the scalp the only lesion found is an area of hyperemia above the right mastoid prominence. Here the scalp is scaly with a large amount of dandruff.

It is notable that the skin over the bony prominences, particularly over clavicles, scapulae, etc., shows circumscribed patches of deeper eschar formation.

The areolæ of the nipples show strikingly the greater intensity of the injury around the hair follicles and sebaceous glands. Each nipple is surrounded by a deep zone of hyperemia in which the epidermis has been lost; through the hyperemic skin the yellowish, enlarged hair follicles can be seen.

The skin of penis and scrotum is discolored, necrotic, and gives a foul gangrenous odor. There is a well-marked phimosis, but the small portion of the glans exposed, around the meatus, is necrotic, yellowish, and infiltrated with pus. A drop of pus exudes from the meatus. The remaining portion of the mucosa of the glans shows a marked inflammatory reaction (hyperemia, infiltration, and edema). Through the discolored skin of the scrotum the yellowish necrotic enlarged hair follicles and sebaceous glands stand out prominently. Around the anus there is a zone of marked gangrene and suppuration of the skin.

The areas of skin (face, hands, legs, and feet) not affected by the lesions show marked anemia.

Mucous membranes.—These are pale, particularly the lips. They are dry but show no burns. Tip of the tongue shows no lesions. (See *infra*.)

Eyes.—The cornea and conjunctivæ of both eyes are clear; there is no hyperemia, no discharge, no opacity. No signs at all of conjunctival involvement.

Nose.—Nasal openings negative.

Ears.—Auditory passages negative.

Edema.—Trace only about ankles; none in eyelids or below eyes. Over the burned areas the skin is swollen, tumefied, infiltrated, consistency increased, but pits only slightly on pressure.

Main section.—On section the panniculus is abundant, pale yellow, moist shining, and only slightly edematous. The superficial veins are markedly anemic. No free gas in peritoneal cavity. Abdominal recti deep red in color, with lighter patches of hyaline or Zenker's necrosis (as in typhoid). Omentum lies a hand breadth below the umbilicus, is very rich in fat; its vessels are empty.

There is no free fluid in the cavity. The peritoneal surface is clear, shining, rather dry, but shows no signs of inflammation. Upper coils of small intestine are distended with gas. Cecum is greatly distended, also transverse colon, and descending colon as far as the sigmoid.

Hepatic and splenic flexures collapsed.

Stomach in normal position, contains a small amount of fluid and gas. Vessels of stomach enormously congested. Pylorus is in normal position. Old adhesions around the appendix, but no active process. The appendix is 10 cm. long, patent throughout, and empty.

Lower border of liver in median line is three finger breadths below the ensiform, and about one finger breadth below costal margin in the right nipple line. The spleen is in normal position, the lower pole about two fingers above the costal margin.

The diaphragm on the left is in the fifth intercostal space, and at the fifth rib on the right.

The thoracic muscles are deep red, very dry, and anemic.

The costal cartilages are white, and cut easily.

No free gas or fluid in the pleural cavities.

The sternum shows normal consistence, and its red marrow is in normal amount and appearance.

The anterior mediastinal fat is very abundant and shows numerous petechial hemorrhages. The fat is very abundant over the pericardial sac, and shows numerous petechial hemorrhages.

The thymic fat is abundant and contains numerous petechial hemorrhages. In it, the thymus is still present in the form of two distinct lobes, each of which is 5 cm. long and 3 to 5 mm. thick. Its color is pink, consistence firm; no hemorrhages in its substance.

The lungs meet in the middle line above the heart. The apex of the heart is in the fifth intercostal space inside the left nipple line.

Both lungs are free throughout. There is no fluid in either pleural cavity.

Pericardium.—No gas in pericardial sac; fluid normal in amount, clear amber. Pericardial lining smooth, clear, moist, shining.

Heart.—Heart is small, smaller than cadaver's right fist; in marked rigor mortis, the left ventricle completely contracted, and the right one nearly so. The auricles and venæ cavae are collapsed, nearly empty; on section, contain but a small amount of dark fluid blood. The subepicardial fat is in excess; over the pulmonary artery, just above the conus, is a sclerotic patch ("soldier's spot") about the size of a dime; along the coronary branches, posteriorly over the left ventricle, are narrow stripes of sclerosis. There are numerous subepicardial hemorrhages, most marked in the neighborhood of the auriculoventricular groove. On section the heart contains a very little fluid blood and small thin lardaceous agonal clots, particularly in the right ventricle, extending into the pulmonary artery.

The mitral opening admits two fingers; the flaps are negative. In the left auricle a small agonal lardaceous clot. The left ventricle wall measures 20 mm. in thickness, the muscle is deep brownish-red, firm, and shows no cloudiness, fibroid patches, or fatty change. No fatty change seen beneath the endocardium,

The tricuspid opening admits three fingers barely. Its flaps are normal. Small agonal clot in right auricle. The foramen ovale is patent, an oval slit admitting probe 3 mm. in diameter, but well guarded by membranous curtain. The pulmonary artery admits two fingers, the pulmonary semilunar valves are negative. The right ventricle wall measures 3 to 8 mm. in thickness, about one-half of this being fat tissue. The aortic opening admits the thumb easily. Its semilunar flaps negative. The beginning of the aorta shows very fine stripes and patches of fatty degeneration of the intima. Arch of aorta negative; also its main branches. Pulmonary artery and main branches empty and negative.

(For protocol of lungs, see p. 611.)

Examination of thoracic duct negative.

Thoracic aorta shows linear stripes of fatty degeneration.

(For protocol of mouth and neck organs, see p. 611.)

The cervical esophagus shows some injection of its mucosa at its mouth, with superficial desquamation; below this no changes except post-mortem hypostasis. A small amount of stomach contents in the lower portion.

The thyroid is small, but on section shows normal amount of colloid.

Parathyroids, four in number, brownish in color, about normal size.

Cervical nodes are about normal in size, some larger, translucent, slightly edematous.

Parotid and submaxillary glands are normal in size and appearances.

Great vessels and nerves of neck region are negative.

Abdominal organs.—The spleen is somewhat enlarged, soft, flattens on the board, its capsule slightly wrinkled. On its surface are the remains of a few old adhesions to the diaphragm. On section the pulp is soft, deep brownish-red, rises above the trabeculae, the cut surface slightly shagreened. Bleeds rather poorly. Follicles barely visible. There are no infarcts, abscesses, or other lesions apparent.

The adrenals are surrounded by abundant fat tissue. Both are normal in size, the cortex pale yellow and somewhat fatty, the medullary portions showing no post-mortem changes. No pathologic changes apparent.

The kidneys have large fatty capsules. Fibrous capsules strip very easily. Both kidneys somewhat enlarged, plump, and markedly congested. Surfaces smooth, veins congested. On section both kidneys bleed freely. The cut surface shows extreme congestion; the outlines between labyrinths and medullary rays are not distinct. The surface is slightly cloudy (slight or moderate cloudy swelling). The pelvis of the left kidney is negative; that of right is dilated, filled with cloudy urine, and its mucosa slightly injected.

The left ureter is normal in size and appearance; the right is dilated with cloudy urine.

The urinary bladder is moderately distended, containing about 60 to 70 c. c. of turbid urine. Mucosa is pale, negative.

The prostate is of normal size and shape; on section normal in appearance.

The seminal vesicles contain a small amount of thin, brownish semen on the right side; on the left they are nearly empty, and the walls show some thickening.

The testes show congested tunics. No fluid in sacs. On section both organs are rather small, slightly congested, and slightly edematous. The left testis shows slight fibrosis extending from the rete.

(For protocol on gastrointestinal lesions see p. 620.)

The liver is much enlarged, particularly the right lobe; but the lower border is rather sharp. Capsule negative. Surface smooth. Color deep brownish red, with paler anemic areas. On section bleeds very freely. Consistency fairly firm. Cut surface uniform deep reddish-brown, the lobules enlarged, with congested central areas and slightly cloudy parenchyma (slight cloudy swelling). Anemic areas show slight fatty shine.

The bile passages are patent. Gall-bladder small; contains a moderate amount of thick brownish bile; no concretions.

The portal vein, common duct, and inferior vena cava negative on section.

The entire splanchnic area is congested.

The retroperitoneal and mesenteric lymph nodes are enlarged, markedly congested, and somewhat edematous. The prevertebral hemolymph nodes are hyperplastic, deep red, and very numerous.

The thoracic and abdominal aorta small in size (hypoplastic), empty; the intima shows linear stripes of fatty degeneration, most marked in the neighborhood of the celiac axis.

Semilunar ganglia and solar plexus negative.

Nervous system.—The scalp is negative except for changes mentioned above. Periosteum of cranium negative. In the right parietal bone a circular area of slight hyperostosis resulting from a cephalhematoma at birth. Corresponding to this area of elevation there is on the inner surface of the skull cap a marked paechionian depression almost perforating the greatly thinned outer table. The skull cap is thin; dura adherent all over; the meningeal grooves and paechionian depressions unusually marked for age of cadaver; the lamina vitrea rough and dull; the dura is thickened throughout. The arachnoid shows numerous focal thickenings; the subarachnoid fluid is markedly increased (edema); no evidences of inflammation. Central longitudinal sinus is negative. The basal meninges are slightly thickened and unusually tough.

The basal vessels are negative.

The entire leptomeninges are somewhat thickened, but strip easily.

The cerebral convolutions are rather sharp, but show no focal lesions. The ventricles are somewhat dilated; the cerebrospinal fluid is increased greatly, but is clear. The ependyma is normal.

The chorioid plexus is markedly congested on both sides. The pineal gland is normal in size and appearance. On section the cerebrum shows congestion and edema. No hemorrhages found. The cerebellum shows marked congestion and edema. Dentate nuclei are normal. No lesions in cerebellar lobes. The basal ganglia, internal and external capsules, are negative.

The pons and medulla are congested and edematous. No lesions apparent.

The cervical cord shows slight congestion and edema. No lesions apparent.

The hypophysis is of normal size, congested.

Basal sinuses congested. Base of skull negative.

PROVISIONAL GROSS PATHOLOGIC DIAGNOSIS

Mustard-gas burns of skin and upper respiratory tract; gangrene and secondary infection of skin; shock; toxemia; edema, congestion, and early hemorrhagic bronchopneumonia. Passive congestion of all organs. Splanchnic congestion marked. Moderate parenchymatous degeneration of kidneys and liver (toxic); multiple petechial hemorrhages; congestion and edema of brain and cord; thymicolymphatic constitution.

MICROSCOPIC FINDINGS

Cerebrum.—Sections taken from all parts of the cerebral cortex, basal ganglia, floor of ventricles, internal capsule, show intense congestion, edema and a few minute perivascular hemorrhages.

Pons, medulla, and cerebellum.—Show a similar congestion and edema.

Meninges.—Old thickenings. No active process. Marked congestion of the vessels and edema. In the larger pial veins there are agonal clots rich in leucocytes.

Hypophysis.—Intense congestion; otherwise negative.

Pineal gland.—Large calcareous concretion. Gland substance smaller in amount than normal. Marked edema.

Spinal cord.—Edema. Congestion. Post-mortem myelinosis.

Heart.—Subepicardial fat abundant. Vessels congested. Numerous petechial hemorrhages throughout the fat. Heart muscle fibers somewhat smaller than normal—acute simple atrophy. Stroma somewhat increased around the coronaries in the left ventricle wall. Endocardium is negative. Heart muscle shows very slight parenchymatous degeneration. No fat. Mixed agonal clots taken from the heart show white clot with very few leucocytes, while in the red portions of the clot there are large collections of leucocytes.

Aorta.—Stripes of marked fatty degeneration in the intima. These are longitudinal and stain rather brownish-red with sudan III and also a brownish-red with scarlet-red. Osmic acid not successful.

(For respiratory tract and neck organs, see p. 611.)

Thyroid.—Vessels congested. Otherwise negative.

Cervical lymph nodes.—Show marked sinus catarrh with numerous hemophages in the sinuses. The cervical hemolymph nodes show marked congestion and hemolysis, many hemophages in the sinuses.

Thymus.—Remains of thymus scattered throughout the thymic fat with large corpuscles of Hassall, many of which are calcified.

Spleen.—Marked acute passive congestion. Small hemorrhages scattered throughout the pulp. Acute lymphoid exhaustion. Follicles very small with central exhaustion. No degeneration of the central portion of the follicles seen as in burns of the skin. No thrombi, no emboli or infarcts.

Adrenals.—Slight cloudy swelling of the cortex. No increase in fat content. Congestion. Edema. Chromaffinic substance small in amount.

Kidneys.—Intense congestion. Cloudy swelling, particularly of the convoluted tubules. Numerous small precipitates of phosphates in the straight tubules of the cortex (concentrated urine). Marked edema of the connective tissue around the larger vessels and of the medullary portion. Very few casts. Frozen sections show no fat.

Bladder.—Congestion and edema. Otherwise negative.

Prostate.—Congestion. Gland spaces filled with secretion and desquamated epithelium. No pathologic changes. The prostatic plexus contains an organizing thrombus.

Seminal vesicles.—Negative. The one apparently hyaline shows only collapse of the wall; empty, but no fibrosis.

Posterior urethra.—Negative.

Testes.—Very little normal spermatogenesis. Many atypical division figures and desquamation of spermatids. Stroma is increased throughout, basement membrane thickened. Appearances suggest an old mumps orchitis. Intense congestion of the vessels.

Epididymis.—Negative.

Penis.—Foreskin edematous. Vessels congested, with areas of complete necrosis of the epithelium of the subepithelial tissues. Where the epidermis is intact, the horny layer is thickened and the epithelium beneath shows evidences of regeneration. The glans shows likewise areas of necrotic epithelium with areas of regeneration and other patches in which the horny layer is greatly thickened and adherent. The meatus shows a slight inflammation. The body of the penis shows areas of regenerating epithelium covered with a dense desquamated horny layer. Large areas of the surface are denuded, the epithelium necrotic, the necrosis extending into the subepithelial tissues. Marked congestion and edema throughout the organ and a mild diffuse inflammation.

Liver.—Acute passive congestion. Slight cloudy swelling. Fat stains show no fatty degeneration but a few scattered cells containing large droplets of fat.

Pancreas.—Congestion. Early post-mortem softening. No other pathologic changes. Islands numerous, many of them very large.

Stomach.—Post-mortem digestion of upper part of mucosa. Congestion. Hemorrhages.

Duodenum.—Post-mortem necrosis of mucosa. Marked mucoid change in glands of Brunner.

Small intestine.—Post-mortem desquamation of epithelium. Congestion. Edema. Slight catarrh.

Colon.—Similar changes.

Appendix.—Evidences of old inflammation. No active process.

Mesenteric glands.—Lymphoid hyperplasia, with exhaustion of the germ centers. Marked sinus catarrh. Many hemophages.

Retroperitoneal hemolymph nodes.—Marked congestion of sinuses. Great numbers of hemophages.

Skin.—The skin taken from various portions of the body shows complete necrosis of the epidermis and greater part of the corium reaching as far as the sweat glands over the greater part of the surface, but in many instances reaching the subcutaneous tissues. Many colonies of bacteria are found upon the necrotic corium but there is very little leucocytic infiltration in the necrotic corium or at the border between the living and dead tissues. Only in scattered areas where there is evidently a localized secondary infection are there any notable collections of polynuclears. The vessels in the lower portion of the corium show intense congestion, stasis. In the lymphatics there is a heavy albuminous precipitate with coarse fibrin threads. The lower border of the corium and upper portion of the subcutaneous fat shows usually a well-marked edema. No old thrombi are found and very few hemorrhages, only here and there have a few red blood cells escaped from the vessels. More recent clots with heavy threads of fibrin are found in many of the distended vessels. In these clots many hemolyzed red blood cells are seen. Some hyaline clots are found in the areas of marked necrosis and secondary infection, but these may be secondary to the latter process. Fibroblastic proliferation has begun at the lower border of the necrotic corium and is particularly marked around many of the blood vessels and sweat glands. Regeneration of epithelium from the hair follicles and sweat glands has begun in many areas and in some instances extends to the surface. Separation of the eschar has begun in some areas. Every degree of change is shown from areas where the necrotic epithelium is still adherent, to those areas where the slough is beginning to separate, and to areas of beginning regeneration. A striking feature of the

process is that the sebaceous glands are everywhere completely destroyed, but islands of regenerating squamous epithelium mark the site of these glands. The sweat glands also show marked degeneration, the majority of the acini being necrotic or hydropic. Regeneration of epithelium occurs almost entirely from the hair follicles and ducts of the sweat glands. Around the nipple, in the axillary region, and over the scrotum the necrosis is deeper and more marked and the large sweat glands of the axilla show marked degeneration. In the scrotum the necrosis extends deep into the dartos, involving the superficial bundles of involuntary muscle. In the scrotum, also, regeneration of epithelium proceeds from the hair follicles.

FINAL PATHOLOGIC DIAGNOSIS

Mustard-gas burns of skin and upper respiratory tract. Necrosis, secondary infection and gangrene of skin. Acute necrotic pharyngitis. Acute catarrhal laryngitis, tracheitis, and bronchitis. Congestion and edema of the lungs. Acute passive congestion of all organs. Multiple petechial hemorrhages. Marked fatty degeneration of intima of aorta. Parenchymatous degeneration of kidneys and liver. Splanchnic congestion. Shock. Toxemia. Secondary anemia. Hypoplasia of heart and aorta. Thymicolymphatic constitution. Hyperplasia of hemolymph nodes with excessive hemolysis. Organizing thrombus in prostatic plexus. Old orchitis (mumps?).

SUMMARY OF CASE

The pathologic findings in this autopsy case give no evidence of a systemic action of dichlorethylsulphide. All of the changes seen can be explained as due to the direct local action of the mustard-gas vapor or as secondary to the shock and secondary infection of the lesions.

GENERAL PATHOLOGY RESULTING FROM SUBCUTANEOUS AND INTRAVENOUS INJECTIONS OF DICHLORETHYLSULPHIDE

Series of animals, rabbits and dogs, were given varying amounts of dichlorethylsulphide by subcutaneous and intravenous injection. Two samples of very pure dichlorethylsulphide were used, one furnished by the chemical laboratory of the University of Michigan, and the other by the Chemical Warfare Service. For the subcutaneous injections in rabbits, a site on the right side of the back was constantly employed. The hair was clipped or shaved over an area 6 cm. in diameter and the liquid dichlorethylsulphide was injected into the subcutaneous fascia above the spinal muscles. In dogs, also, the injection was made beneath the skin of the back. For the intravenous injections in rabbits, the superficial femoral and jugular veins were used. The pure substance was used, instead of oily solutions, because of the great danger of fatty embolism with the latter. In most cases, the animals were allowed to die, but some were killed in order to avoid post-mortem change in the tissues. In all cases autopsies were done, the tissues were fixed in formol, and sections of all organs were stained in hematoxylin and eosin and other routine stains.

SUBCUTANEOUS INJECTION OF DICHLORETHYLSULPHIDE

The following condensed protocols are selected as representative of the reactions following injection of varying amounts of dichlorethylsulphide. Rectal temperatures, daily weights and character of feces are given, and these, taken together, serve to indicate the severity of the reaction.

PROTOCOLS

RABBIT 55.—Subcutaneous injection of 0.015 c. c. of dichlorethylsulphide. Very slight general reaction, with apparently complete recovery, except for the local lesion, 26 days after injection.

Date	Temperature (degrees)	Weight, in grams	Notes
Dec. 16.....	102.3	1,870	0.015 c. c. dichlorethylsulphide subcutaneously.
17.....	102.5	1,750	No diarrhea.
18.....	102.7	1,740	Do.
19.....	102.6	1,870	Do.
20.....	103.1	1,880	Do.
21.....	102.6	1,930	Do.
22.....	102.6	1,950	Slight diarrhea.
23.....	103.2	2,010	No diarrhea.
24.....	103.5	1,970	Do.
25.....	102.6	2,010	Do.
26.....	102.6	2,060	Do.
27.....	103.0	2,100	Do.
28.....	103.3	2,200	Do.
29.....	104.1	2,090	Do.
30.....	103.4	2,200	Do.
31.....	103.1	2,130	Do.
Jan. 1.....	102.8	2,120	Do.
2.....	103.3	2,070	Do.
3.....	103.0	2,140	Do.
4.....	102.6	2,150	Do.
5.....	103.3	2,130	Do.
6.....	102.8	2,090	Do.
7.....	103.0	2,090	Do.
8.....	103.4	2,090	Do.
9.....	103.5	2,150	Do.
10.....	102.2	2,300	Do.
11.....	102.8	2,190	No diarrhea. Lesion is now nearly healed. There is a hairless area about 1 cm. in diameter, which is covered with a shiny smooth cicatrix except for a small area in its central portion.

RABBIT 48.—Subcutaneous injection of 0.03 c. c. of dichlorethylsulphide. Slight general reaction. Living, 37 days after injection, with apparent complete recovery, except for the local lesion.

Date	Temperature (degrees)	Weight, in grams	Notes
Dec. 5.....	101.6	2,100	0.03 c. c. dichlorethylsulphide subcutaneously. No signs of local irritation.
6.....	102.6	2,020	No diarrhea. Animal very thirsty.
7.....	102.0	2,050	Do.
8.....	103.0	2,060	Do.
9.....	101.0	1,990	Do.
10.....	101.8	1,940	Slight diarrhea.
11.....	103.6	1,950	No evidence of diarrhea.
12.....	102.4	1,990	Perianal hair somewhat soiled.
13.....	103.6	1,900	No diarrhea.
14.....	104.4	1,870	Do.
15.....	103.9	2,000	Do.
16.....	103.2	2,030	Do.
17.....	102.7	1,930	Do.
18.....	102.6	1,830	Do.
19.....	101.6	1,810	Do.
20.....	102.6	2,040	Do.
21.....	103.6	2,000	Do.
22.....	102.2	2,080	Do.
23.....	102.1	2,110	Do.
24.....	102.7	2,090	Do.
25.....	103.3	2,000	Do.
26.....	101.6	2,060	Do.
27.....	102.0	2,070	Do.
28.....	102.3	2,150	Do.
29.....	103.5	2,110	Do.
30.....	103.7	2,140	Do.
31.....	103.6	2,170	Do.
Jan. 1.....	103.1	2,020	Do.
2.....	102.9	2,030	Do.
3.....	102.8	2,250	Do.
4.....	103.5	2,170	Do.
5.....	103.2	2,060	Do.
6.....	103.4	2,020	Do.
7.....	103.2	1,990	Do.
8.....	102.1	2,020	Do.
9.....	102.6	2,060	Do.
10.....	102.8	2,240	Do.
11.....	102.6	2,100	No diarrhea. The local lesion is not yet completely healed. There is an indurated area about 1 by 1.5 cm. over which there is an incomplete regeneration of epithelium. This area is firmly adherent to the underlying tissue.

RABBIT 47.—Subcutaneous injection of 0.03 c. c. of dichlorethylsulphide. Moderately severe reaction. Death on the twelfth day.

Time	Temperature (degrees)	Weight, in grams	Notes
Dec. 5.....	102.5	1,520	0.03 c. c. dichlorethylsulphide subcutaneously. No evidence of local reaction.
6.....	102.8	1,430	No diarrhea.
7.....	102.1	1,490	No diarrhea. Edematous area at site of injection measures 2 by 6 cm.
8.....	101.8	1,460	No diarrhea.
9, 9.30 a. m.....	97.6	1,380	Do.
9, 10.30 a. m.....	97.0	-----	Hair soiled about anus and soft fecal material on thermometer.
10, 9.30 a. m.....	98.6	1,250	Diarrhea.
10, 5 p. m.....	96.0	-----	Do.
11, 9 a. m.....	99.0	1,120	Do.
11, 5 p. m.....	96.7	-----	Do.
12, 9.30 a. m.....	99.8	1,155	Do.
12, 4.30 p. m.....	100.2	-----	Hair soiled, but feces formed.
13.....	101.6	1,100	No diarrhea.
14.....	101.5	1,060	Do.
15.....	100.8	1,060	Do.
16.....	101.7	1,070	Do.
17.....	97.2	995	Appears much sicker. Perianal hair soiled, but no diarrhea noted.
17, 1 p. m.....	-----	-----	Died.

Autopsy.—Autopsy at 1.45 p. m. Body warm. No rigor. Pleural cavities and pleurae negative. Heart contracted. The right auricle still pulsates when stimulated. The lungs show a moderate congestion, with hypostatic areas posteriorly in the lower lobes. The liver is congested; otherwise negative. The gall-bladder is not distended. The spleen shows a moderate congestion, likewise the kidneys, in which there are also some edema and slight cloudy swelling. The stomach is nearly empty and the mucosa shows no changes. The upper small intestines are slightly edematous. Formed stools are found in the colon. No evidence of diarrhea. At the root of the mesentery there is a lobulated mass of edematous hyperplastic lymph nodes.

Microscopic findings.—Lungs: Slight congestion. No edema. Heart: Negative. Spleen: Congestion. In the sinuses are great numbers of pigmented hemophages, the pigment varying in color from brown to almost black. Hemosiderosis. Kidneys: Moderate congestion. Very slight cloudy swelling. Practically negative. Adrenals: Negative. Stomach: Negative. Small intestine: Congestion and edema of mucous membrane with necrosis of the superficial epithelium of the tops of the folds and villi. Glands of Lieberkühn show excessive mucus formation and individual glands show necrosis. Minute erosions occur along the mucosa. Liver shows marked passive congestion; a nutmeg liver with acute central necrosis in many lobules. The bile-ducts show an unusual mucous degeneration of the epithelium, with edema of the surrounding connective tissue. There is a complete necrosis of the epithelium of the gall-bladder and of its basement membrane. The neighboring liver tissue also shows a zone of necrosis as from the diffusion of some necrosing substance from the gall-bladder. At the site of injection there is a large area of necrosis extending through the striped muscle into the fascia. About this there is a zone of fibroblastic proliferation and leucocyte infiltration. The striped muscle in the neighborhood shows a marked Zenker's necrosis.

RABBIT 50.—Subcutaneous injection of 0.06 c. c. of dichlorethylsulphide. Moderately severe reaction. Apparent recovery, except for local lesion. Animal killed on the thirty-second day after injection.

Time	Tem- perature (degrees)	Weight, in grams	Notes
Dec. 6.....	101.7	2,020	0.06 c. c. dichlorethylsulphide subcutaneously.
7.....	101.8	2,000	No diarrhea. Very thirsty.
8.....	101.6	2,130	No diarrhea.
9.....	100.0	2,060	Do.
10, 9.30 a. m.....	100.9	1,990	Do.
10, 5 p. m.....	98.6	-----	Perianal hair somewhat soiled.
11, 9 a. m.....	100.0	1,920	Diarrhea.
11, 5 p. m.....	98.6	-----	Marked foul diarrhea.
12, 9.30 a. m.....	99.6	1,840	Diarrhea.
12, 4.30 p. m.....	101.7	-----	Perianal hair still soiled.
13.....	102.6	1,790	Do.
14.....	102.6	1,840	Stool slightly soft.
15.....	102.4	1,820	Do.
16.....	102.7	1,840	Perianal region still somewhat soiled.
17.....	101.8	1,710	No diarrhea.
18.....	102.0	1,650	Do.
19.....	102.3	1,640	Do.
20.....	102.2	1,740	No diarrhea. Quite weak.
21.....	103.0	1,710	Do.
22.....	101.8	1,660	No diarrhea. Weak and appears very sick.
23.....	102.9	1,680	No diarrhea. Appears stronger.
24.....	103.0	1,650	Do.
25.....	103.2	1,680	Do.
26.....	102.6	1,740	Do.
27.....	104.0	1,780	Do.
28.....	102.7	1,800	Do.
29.....	102.9	1,810	Do.
30.....	103.9	1,910	Do.
31.....	103.6	1,950	Do.
Jan. 1.....	103.6	1,900	Do.
2.....	103.4	1,870	Do.
3.....	102.9	1,910	Do.
4.....	103.2	2,030	Do.
5.....	102.9	1,940	Do.
6.....	102.7	1,930	Do.
7.....	102.9	1,970	No diarrhea. The local lesion now measures 15 by 30 mm. It is dry, non-purulent and shows slowly progressing healing.
7, 2.30 p. m.....	-----	-----	Animal killed. Autopsy at once.

Autopsy.—Pleuræ, pleural cavities, heart, and lungs are negative. The stomach is distended with food; its mucosa appears negative. The gall-bladder is small; the bile, pale. Liver: Congestion. Spleen: Congestion. Kidneys: Slight cloudy swelling and congestion. The upper small intestines contain a small quantity of thin fluid material. There are no formed stools in the colon, but no evidence of diarrhea. The intestinal mucosa shows no lesions to the naked eye.

Microscopic findings.—Heart: Negative. Lungs: Congestion without edema. Small patches of bronchopneumonia. Spleen: Marked congestion with a fairly large number of pigmented phagocytes. Kidneys and adrenals: Negative. Stomach: Negative. Mucosa well preserved. Liver: Congestion. Slight cloudy swelling. Bile-ducts negative. Gall-bladder: Epithelium well preserved. No necrosis. Intestine: Marked catarrhal enteritis. Epithelium well preserved. No desquamation. Lumen nearly empty. Pancreas: Congestion. Mesenteric lymph nodes. Extreme edema.

RABBIT 63.—Subcutaneous injection of 0.08 c. c. of dichlorethylsulphide. Severe reaction. Animal killed on the fifteenth day.

Date	Temper- ature (degrees)	Weight, in grams	Notes
Dec. 23.....	105.0	2,810	0.06 c. c. dichlorethylsulphide in deep subcutaneous and intramuscular injection.
24.....	103.6	2,770	No diarrhea.
25.....	103.0	2,580	Do.
26.....	102.0	2,610	Slight diarrhea.
27.....	102.1	2,580	Diarrhea.
28.....	99.7	2,500	Do.
29.....	98.5	2,450	Marked diarrhea.
30.....	100.9	2,260	Do.
31.....	101.6	2,120	Do.
Jan. 1.....	101.8	2,130	Diarrhea.
2.....	103.0	2,050	Stools formed but moist. Marked edema of right half of abdominal wall.
3.....	102.9	2,060	No diarrhea.
4.....	103.4	2,100	Do.
5.....	103.1	1,950	Do.
6.....	102.0	1,920	Do.
7.....	100.5	1,840	Do.
7, 1.30 p. m.....	-----	-----	Killed. Autopsy at once.

Autopsy.—Pleural cavities, pleuræ, heart and lungs negative, except for numerous firm, slightly caseous areas at root of right lung, probably an old tuberculosis. Peritoneal cavity contains about 50 c. c. of clear fluid. Liver: Congestion. Gall-bladder: Moderately distended with thin bile. Stomach: Moderately filled. No visible lesions of the mucosa. Intestines: Peristalsis very active. Thin mucoid fluid in upper small intestine. In the cæcal pouch there is much thick gruel-like fecal material with denser oval masses adherent to the mucosa. Formed stools in color. Kidneys: Congestion and slight cloudy swelling. Adrenals: Congestion. Mesenteric nodes: Somewhat hyperplastic.

Microscopic findings.—Heart: Negative. Lungs: Pulmonary abscesses. Congestion. Spleen: Marked congestion. No pigmented phagocytes. Kidneys: Congestion, otherwise negative. Adrenals: Excess of fat. Marked lipoidosis of fascicular and reticular zones. Stomach: Negative. Intestines: Epithelium well preserved for the greater part. No mucoid degeneration except in one portion, where the mucous glands are distended and filled with hyaline cast-like masses. Many of the glands are shallow mucous cysts. Liver: Cells small, simple atrophy. Gall-bladder: Epithelium perfectly preserved. No necrosis. Papillæ less marked than normal. Submucosa edematous. Site of injection: Large area of necrotic muscle. Deposit of lime salts. Bacterial infection.

RABBIT 65.—Subcutaneous injection of 0.12 c. c. of dichlorethylsulphide. Very severe reaction. Death on the fifth day.

Time	Temperature (degrees)	Weight, in grams	Notes
Dec. 23.....	104.3	2,750	0.12 c. c. dichlorethylsulphide subcutaneously.
24.....	104.9	2,580	No diarrhea.
25.....	102.0	2,470	Beginning diarrhea.
26.....	102.8	2,410	Diarrhea.
27.....	100.8	2,310	Slight diarrhea.
28.....	97.2	2,200	Very severe diarrhea. Died during the night of Dec. 28 to 29.

Autopsy.—Body cold. Marked rigor. Entire posterior portion of body is soaked with fluid feces. At the site of injection there is a small brownish area. On incising this area the subcutaneous fascia is found to be a bright sulphur yellow in color. There is very little local edema. Pleural cavities and pleuræ are negative. The heart shows a slight dilatation. There is a moderate congestion of the lungs most marked posteriorly. The peritoneum is negative and there is no fluid in the abdominal cavity. The liver is firm, deeply fissured, and shows a marked congestion. The gall-bladder is nearly empty, collapsed, its wall wrinkled. It contains but a few drops of a thin yellowish mucoid fluid. The stomach is moderately distended. The stomach mucosa appears negative. The spleen and kidneys show congestion; otherwise they are negative. Adrenals: Negative. The intestines contain only fluid fecal material. No lesions of the intestinal tract can be seen. All splanchnic veins show a marked congestion.

Microscopic findings.—Heart: Negative. Large white clot in right ventricle. Lungs: Intense congestion and edema. Patches of atelectasis. One of the pulmonary arteries contains a large laminated thrombus or embolus, rich in leucocytes. Spleen: Intense congestion. In the sinuses there are great numbers of phagocytes containing hemosiderin. Kidneys: Congestion, otherwise negative. Adrenals: In one adrenal there is an area of fibrosis. Liver: Intense congestion. Cloudy swelling. Cirrhosis. Coccidiosis. Gall-bladder is completely necrotic. Necrotic diffusion zone in surrounding liver tissue. The larger bile-ducts show hyaline swelling of their columnar epithelium. Excessive mucus formation. Stomach: Post-mortem change, otherwise negative, except at the pyloric end, where there is a marked mucoid degeneration. Intestine: Extreme catarrh. All glands show extreme mucous degeneration. Desquamation of the epithelium. Skin lesion: Large area of necrosis. Hemorrhage. Edema. No reaction.

RABBIT 64.—Subcutaneous injection of 0.12 c. c. of dichlorethylsulphide. Severe reaction. Death on sixth day. The close parallelism between this case and the preceding is noteworthy.

Date	Temperature (degrees)	Weight, in grams	Notes
Dec. 23.....	103.7	2,500	0.12 c. e. dichlorethylsulphide subcutaneously.
24.....	103.5	2,260	No diarrhea. Some edema of abdominal wall on the right side.
25.....	103.1	2,210	No diarrhea. Edema continues.
26.....	103.4	2,110	Do.
27.....	103.4	2,040	Moderate diarrhea.
28.....	103.2	1,920	Slight diarrhea.
29.....	97.6	1,830	Marked diarrhea. Died during the night of Dec. 29 to 30.

Autopsy.—Body cold. No rigor. Edema of abdominal wall has diminished. There is a small red-brown eschar at the site of injection. Heart: Moderate dilatation. Fibrin and leucocyte clot in right auricle. Lungs are somewhat mottled, particularly in upper lobes, probably an early lobular pneumonia. Congestion. Peritoneum: Moist, shining. Liver: Congested. Gall-bladder: Well filled. Bile, thin and greenish-yellow in color. Small intestines and greater part of colon distended with very abundant yellowish-brown fluid fecal material. Formed stools in descending colon. Kidneys: Moderate congestion. Splanchnic vessels all show marked congestion.

Microscopic findings.—Heart: Negative. Large white clot with very few leucocytes. Lungs: Purulent bronchopneumonia. Marked congestion and edema. There is a large thrombus in a pulmonary vessel, the wall of which shows necrosis. Around the vessel there is a zone of necrosis which shades off to partial necrosis, as though due to the diffusion of a necrosing substance from the vessel. There are enormous numbers of staphylococci throughout the lung. Kidneys: Congestion. Numerous casts in one. Gall-bladder: Wall completely necrosed, with area of diffusion necrosis in surrounding liver tissue. Liver: Congestion. Cloudy swelling. Small areas of lime salt deposit in necrotic liver cells. Some of the larger bile-duets show a polynuclear infiltration around the columnar epithelium. The epithelium itself shows a slight cloudy swelling. Adrenals: Increased lipoid content in cortex. Congestion of medulla. Stomach: Negative. Intestines: Marked desquamative catarrh. Necrosis of upper portion of mucosa. Extreme mucoid degeneration of the glands. Site of injection: Enormous area of necrosis extending clear through the skin and subcutaneous tissues. Hemorrhage. Thrombosis. Areas of polynuclear infiltration. Secondary infection.

RABBIT 67.—Subcutaneous injection of 0.18 c. e. of dichlorethylsulphide. Very severe reaction. Severe diarrhea within 24 hours and death during the third day.

Time	Temperature (degrees)	Weight, in grams	Notes
Dec. 27, 3.30 p. m.....	102.2	1,660	0.18 c. e. dichlorethylsulphide subcutaneously.
28, 11 a. m.....	98.2	1,570	Marked diarrhea. Died during the night of Dec. 28 to 29.

Autopsy.—Body cold. Rigor mortis present. Head retracted. Fur about the anus is wet with liquid feces. The abdominal wall shows a marked edema which extends up the right flank. At the site of injection the subcutaneous tissues show but very little edema and no surface lesion is visible. Upon incising this area the fascia is found to be yellow in color. Pleural cavities and pleuræ are negative. Heart: Moderate dilatation. Blood coagulated. Lungs: Marked congestion. Peritoneum: Moist, shining. No free fluid in peritoneal cavity. Liver: Congestion. Gall-bladder: Moderately filled with thin bile. The stomach is partly distended. Its wall is somewhat edematous and in the mucosa several minute erosions are visible. Spleen and kidneys: Congestion. Adrenals: Negative. The intestines are distended with gas and fluid feces. Marked diarrhea. Splanchnic congestion.

Microscopic findings.—Heart: Negative. Lungs: Congestion. Some edema. Areas of atelectasis. Spleen: Congestion without pigmentation. Kidneys, adrenals, and pancreas: Negative. Liver: Congestion. Slight cloudy swelling. The larger bile-duets show desquamation of the epithelium and some of them are completely necrosed. Gall-bladder: The wall is completely necrosed and there is some necrosis from diffusion into the surrounding liver tissue. Stomach: Negative. Intestines: Catarrhal enteritis. Marked mucoid degeneration throughout.

RABBIT 66.—Subcutaneous injection of 0.18 c. c. of dichlorethylsulphide. Severe diarrhea. Marked fall in temperature. Death on the eleventh day.

Date	Temperature (degrees)	Weight, in grams	Notes
Dec. 27	103.7	2,550	0.18 c. c. of dichlorethylsulphide subcutaneously.
28	102.0	2,350	No diarrhea. Marked edema of abdominal wall.
29	101.6	2,320	Do.
30	101.0	2,260	Do.
31	99.6	2,200	Do.
Jan. 1	99.4	2,160	Do.
2	98.0	2,160	No diarrhea. Edema somewhat less.
3	97.0	2,080	Diarrhea.
4	97.1	1,890	Marked diarrhea.
5	95.0	1,610	Marked diarrhea. Left eye sealed with exudate. (Terminal secondary infection.)
6	94.0	1,540	Marked diarrhea. Both eyes sealed with mucopurulent exudate. Died during the night of Jan. 6 to 7.

Autopsy.—Body still warm. No rigor. Both eyes sealed with exudate. When lids are separated, a large quantity of mucopurulent exudate escapes. No superficial lesion at site of injection and only a slight subcutaneous induration can be felt. There is a firm mass, about 2.5 cm. in diameter, in the abdominal wall at the site of the marked edema noted while the animal was living. On incising this mass it is found to be somewhat edematous still, and the tissues are stained a bright sulphur-yellow color. Heart: Right-sided dilatation. Lungs: Pale pink in color. Slight congestion. Liver: Marked congestion. Gall-bladder: Distended. Bile highly pigmented. Stomach: Nearly empty; its contents bile stained and very mucoid. In the mucosa there are numerous small erosions, particularly in the fundus, along the greater curvature. These are covered with an abundant mucus and have shreds of brownish-red material, probably blood clot, streaking the mucus over them. Spleen: Negative. Kidneys: Congestion and slight cloudy swelling. The intestines contain gas and a small quantity of fluid material. There are no formed stools. Adrenals: Congestion.

Microscopic findings.—Heart: Negative. Lungs: Moderate congestion. Emphysema. No edema. Kidneys: One kidney shows many casts in the medullary tubules. Otherwise negative. Spleen: Markedly congested, with a fairly large number of pigmented phagocytes. Liver: Congestion and cloudy swelling. Stomach: Extreme mucoid degeneration of the epithelium of the outer portion of the mucosa, with desquamation. Marked cloudy swelling of the parietal cells. Small post-mortem erosions. Gall-bladder: Mucosa fairly well preserved. No necrosis of wall or neighboring liver tissue. Intestines: Marked mucoid degeneration. Extreme catarrhal enteritis.

RABBIT 69.—Subcutaneous injection of 0.24 c. c. of dichlorethylsulphide. Diarrhea. Death within 12 hours.

Time	Temperature (degrees)	Weight, in grams	Notes
Dec. 30, 3.45 p. m.	103.9	1,660	0.24 c. c. of dichlorethylsulphide subcutaneously. No evidence of local irritation. Died during the night of Dec. 30 to 31.

Autopsy.—Body cold. Rigor present. Soft formed stools matted in hair about anus. No superficial lesion at site of injection, only a slight subcutaneous edema. Upon incising this area there is a very strong odor of dichlorethylsulphide. Heart: Marked dilatation. Lungs: Congestion, with small hemorrhages beneath the pleura of the diaphragmatic surfaces of the lower lobes. Liver: Congestion. Stomach: Moderately distended. No lesions of mucosa visible. Spleen, kidneys, and adrenals: Congestion, otherwise negative. Intestines: Distended with gas and fluid fecal material. No formed stools. Marked splanchnic congestion.

Microscopic findings.—Heart: Negative. Lungs: Congestion. Edema. Small capillary hemorrhages. Adrenals: Negative. Spleen: Congestion. No pigmented phagocytes. Pancreas: Negative. Kidneys: Rather marked cloudy swelling, even to simple necrosis. Gall-bladder: Complete necrosis of wall, necrosis extending into liver tissue for some distance. Slight cloudy swelling of the liver cells. Stomach: Negative. Intestines: Congestion; otherwise negative. Site of injection: Large area of necrosis. Edema. No reaction.

RABBIT 70.—Subcutaneous injection of 0.30 c. c. of dichlorethylsulphide. Diarrhea. Death within 12 hours.

Time	Temperature (degrees)	Weight, in grams	Notes
Dec. 30, 4.15 p. m.	104.0	1,810	0.30 c. c. of dichlorethylsulphide subcutaneously. No evidence of local irritation. Died during the night of Dec. 30 to 31.

Autopsy.—Body cold. Rigor present. Much soft fecal material about the anus. Strong odor of dichlorethylsulphide when area of injection is excised. Heart: Marked dilatation. Lungs: Congestion, otherwise negative. Liver, spleen, kidneys, and adrenals: Congestion. Gall-bladder: Well filled. Intestines: The upper portion of the small intestine is filled with yellowish fluid material. No formed stools in lower colon. Marked splanchnic congestion.

Microscopic findings.—Heart: Hypertrophy and dilatation. Lungs: Intense congestion and edema. Spleen: Congestion. Very few pigmented phagocytes. Pancreas: Negative. Adrenals: Congestion. Kidneys: Congestion and some cloudy swelling. Liver: Congestion and fatty degeneration. Gall-bladder: Necrosed. Diffusion zone of necrosis in the surrounding liver tissue. Intestines: Epithelium well preserved. Early stage of mucous degeneration; practically every cell filled with mucus and the majority of them intact. Site of injection: Large eschar involving all tissues.

RABBIT 72.—Subcutaneous injection of 0.60 c. c. of dichlorethylsulphide. Death on the second day.

Time	Temperature (degrees)	Weight, in grams	Notes
Dec. 31, 3.15 p. m.	102.7	3,050	0.60 c. c. of dichlorethylsulphide subcutaneously. No evidence of local irritation. Animal eating in 5 minutes.
4 p. m.	-----	-----	Sits quietly. Respiration rate appears somewhat accelerated.
6 p. m.	102.5	-----	Quiet. No diarrhea.
7.30 p. m.	102.0	-----	Quiet. Heart regular. Respiration quickened. Seems to be about to roll over on side, but quickly recovers itself.
8.30 p. m.	101.7	-----	No diarrhea.
9 p. m.	101.8	-----	Do.
9.15 p. m.	-----	-----	No diarrhea. Hopping about and eating.
Jan. 1, 10 a. m.	101.1	3,010	No diarrhea.
11 a. m.	102.3	-----	Soft pasty feces.
2.30 p. m.	102.5	-----	Diarrhea. Died during the night of Jan. 1 to 2.

Autopsy.—Body still somewhat warm. Perianal hair soiled. Very strong odor of dichlorethylsulphide at site of injection. Heart: Right-sided dilatation. Lungs: Congestion. Liver, spleen, kidneys, and adrenals: Congestion. Otherwise negative. Stomach: Moderately distended. In the mucosa there are several small erosions with brownish-red bases. Intestines: Much fluid material. No formed stools in lower colon. Diarrhea. Edema of thoracic and abdominal walls.

Microscopic findings.—Brain: Congestion. Heart: Negative. Lungs: Congestion without edema. Spleen: Intense congestion without pigmented phagocytes. Kidneys: Congestion. Otherwise negative. Stomach: Negative. Some post-mortem change. Small intestine: Marked post-mortem change, with the picture of a mucous catarrh involving the greater part of the tract. Liver: Cirrhosis. Coccidiosis. Large bile ducts dilated; their epithelium well preserved. The small bile-ducts are unchanged. Slight fatty degeneration. Gall-bladder: Nearly complete necrosis of wall. Narrow necrotic zone of diffusion into surrounding liver tissue.

RABBIT 74.—Subcutaneous injection of 0.60 c. c. of dichlorethylsulphide, 0.15 c. c. being injected in each of four widely separated areas on the back. Rabbit killed when dying, five hours after injection. An apparent acceleration of reaction with increased opportunity for absorption.

Time	Temperature (degrees)	Weight, in grams	Notes
Jan. 1, 11.45 a. m.	103.5	1,970	0.15 c. c. of dichlorethylsulphide injected in each of four areas. No evidence of local irritation.
2.15 p. m.	-----	-----	Lying on side. Moves legs and head readily. Heart strong and regular. The increased irritability, shown by reaction to sound and jarring of table, suggests that due to strychnine.
4.30 p. m.	-----	-----	Respirations few and gasping. Heart beating vigorously. Diarrhea.
4.45 p. m.	-----	-----	Killed by chloroform. Autopsy at once.

Autopsy.—Head somewhat retracted. Perianal region covered with soft fecal material. Heart: Moderately dilated. Lungs: Negative. Liver: Congestion. Gall-bladder: Nearly empty. Negative. The stomach is moderately distended. The mucosa of the fundus, particularly along the greater curvature, shows a large number of small, shallow erosions with dark red-brown bases. Intestines: Contain much fluid material. No formed stools in colon.

Microscopic findings.—Liver: Marked congestion. Slight cloudy swelling. The small bile-ducts are apparently normal. Gall-bladder: Epithelium perfectly preserved. No changes observable. Stomach: Well preserved. Portions examined show no changes. Intestines: Catarrhal enteritis.

Dog 3.—White bull terrier; weight 8 kilos. Subcutaneous injection of 0.24 c. c. dichloroethylsulphide. Severe diarrhea. Death in four days.

August 27.—0.24 c. c. of dichloroethylsulphide injected subcutaneously in back.

August 28.—Appears sick. Is much less active and coat is roughened.

August 29.—Appears very sick. No diarrhea.

August 30.—Very severe diarrhea. Stools fluid and brownish black in color, resembling altered blood. The animal remains quiet.

August 31, 12 noon.—Lying on side. Respiration slow and shallow. Diarrhea persists. 6 p. m.—Dog died during the afternoon. Autopsy at 7 p. m.

Autopsy.—The body is in complete rigor. The posterior portion is soiled with fluid fecal material. At the site of injection there is an indurated lamellar area, about 10 cm. in diameter, which involves both skin and subcutaneous tissue. Pleural cavities and pleurae negative. Heart: Marked right-sided dilatation, the left ventricle being in rigor. Small amount of very dark fluid blood in the chambers. Lungs: Free throughout; air-containing. Middle lobe of right lung congested. No pneumonia. No free gas or fluid in peritoneal cavity. Omentum free. The subperitoneal vessels over the intestines are congested and there are a few minute subperitoneal hemorrhages. The intestines are empty and firmly contracted. The duodenum contains a bile-stained fluid and the mucosa is bile stained. Throughout the small intestine the mucosa shows a marked congestion and there are small hemorrhages in the summits of some of the folds. The Peyer's patches are hyperplastic. In the colon the mucosa is much congested and there are a few very minute hemorrhages. The appendix is negative. The stomach wall is contracted, the rugae prominent. The mucosa is much congested and there are a few pin-point hemorrhages. The kidneys show slight cloudy swelling. The adrenals were well preserved and negative. The bladder is contracted; its mucosa, negative.

Microscopic findings.—The heart shows dilatation and its vessels are congested. Lungs: Marked edema. Intense congestion. Small hemorrhages. Several areas of hemorrhagic infarction, with embolic blocking of the vessels. Spleen: Congestion. Atrophy. Kidneys: Marked congestion. Slight cloudy swelling. Pancreas: Marked cloudy swelling. Liver: Cloudy swelling. Marked congestion. Marked mucoid degeneration and cloudy swelling of the epithelium of the smaller bile-ducts. All of the bile-ducts contain a violet-staining, hyaline substance and the epithelium is higher than normal, the cells appearing larger and swollen. The nuclei appear increased in number. The cytoplasm stains violet, but many of the cells are vacuolated. In a few of the larger bile-ducts there are small areas of necrosis. The stomach mucosa is intact. There is marked congestion and some increase in mucus in the upper portion of the mucosa. The mucosa of the small intestine is congested, edematous, and infiltrated with leucocytes. The epithelium of the glands shows syncytial formations of regenerating epithelium. The columnar form of the cells is lost and there is no mucus formation except in the lower small intestine, where there are many mucous cysts, especially in the deeper portions of the mucosa. The fundi of the glands of Lieberkühn are dilated, filled with stringy mucin or a colloid material. The epithelium is cuboidal, or flattened, or syncytial, and stains a deep violet with hematoxylin and eosin. In some of the dilated glands of Lieberkühn the epithelium is entirely gone and the lumen is filled with a hyaline cast. The epithelium of the upper part of the glands and of the surface is entirely gone. The picture is that of a severe degenerative and desquamative catarrhal enteritis with beginning regeneration. The lymph follicles are hyperplastic and the germ centers show lymphoid exhaustion. Mesenteric nodes: Marked congestion. Great numbers of hemophages filled with blood cells. Adrenals: Marked congestion of medulla. Site of injection: Large eschar with marked edema. In the vessels there are large thrombi. The borders of the lesion show an abundant polynuclear infiltration and large areas of hemorrhagic extravasation.

SUBCUTANEOUS INJECTION OF HYDROCHLORIC ACID

Since it has been assumed by some that the local and general effects of dichlorethylsulphide are due to the action of the hydrochloric acid produced by its hydrolytic cleavage, a series of animals was given varying amounts of hydrochloric acid by subcutaneous injection. The following protocol is selected as illustrative of this group.

PROTOCOL

RABBIT 76.—Subcutaneous injection of 0.60 c. c. of hydrochloric acid. Both local and general reactions entirely unlike those produced by dichlorethylsulphide.

Time	Temperature (degrees)	Weight, in grams	Notes
Jan. 3, 9.45 a. m.	103.2	1,600	0.60 c. c. of hydrochloric acid subcutaneously. Very marked evidence of local irritation. Marked contraction of superficial and deep muscles. The skin "knots up." In about 5 minutes, evidences of severe pain cease and the animal is eating.
4	103.6	1,710	No diarrhea. Very extensive lesion at site of injection. There has been complete destruction of the skin and subcutaneous fascia over an area 4 by 5 cm. so that the muscles of the back are fully exposed.
5	103.4	1,600	No diarrhea. The muscle is now exposed over an area 5 by 7 cm. There is a constant oozing of blood from the borders of the deeply excavated lesion.
6	103.8	1,490	No diarrhea. Still some bleeding from wound.
6, 8.30 p. m.			Killed by chloroform. Autopsy at once.

Autopsy.—Large excavated lesion, measuring 5 by 7 cm. at the site of injection. The borders are smooth. The base consists of charred, dry, fragmented muscle in coarse bundles and masses. There is no purulent exudate. The whole lesion is nearly black in color, as though charred, and is very foul smelling, with the odor of dry gangrene. Heart: Still beating. Negative. Lungs: Bright pink in color. Moderate congestion. Liver: Congested. Extensive coecidiosis. Spleen: Negative. Stomach: Contains a small amount of food and water, and much swallowed mucus. There are no visible lesions of the mucosa. The intestines are nearly empty except the cecum, which is moderately filled. The scant amount of fecal matter in the small intestine is very thin, mucoid, and bile stained. In the lower colon the fecal material is soft and but slightly formed. There is, however, no evidence of diarrhea about the anus.

Microscopic findings.—Heart: Negative. Lungs: Congestion. No edema and no hemorrhages. Liver: Coecidiosis. No diffusion necrosis into liver tissue around the gall-bladder. Gall-bladder: Epithelium well preserved. No necrosis. No desquamation. Many mucin threads in lumen. Stomach, intestines, kidneys, and adrenals: All negative. Tissue from site of injection: Very extensive eschar formation.

SUBCUTANEOUS INJECTION OF DIHYDROXYETHYLSULPHIDE

A series of animals was given varying doses of dihydroxyethylsulphide (hydrolyzed mustard gas) by subcutaneous injection, in order to ascertain whether the severe general effects could be due to the absorption of this substance from the site of injection. The following condensed protocols are selected from this series.

PROTOCOLS

RABBIT 80.—Subcutaneous injection of 0.30 c. c. of dihydroxyethylsulphide. No local lesion, no diarrhea, and no loss of weight.

Date	Temperature (degrees)	Weight, in grams	Notes
Jan. 8	104.6	2,250	0.30 c. c. of dihydroxyethylsulphide subcutaneously. No evidence of local irritation, and animal eats at once when released.
9	102.8	2,210	No diarrhea. No local lesion.
10	102.6	2,270	Do.
11	102.8	2,240	Do.
12	101.9	2,250	Do.
13	102.6	2,300	Do.
14	102.0	2,300	Do.
15	101.6	2,280	Do.
16	104.0	2,170	Do.
18	103.6	2,18	Do.

RABBIT 81.—Subcutaneous injection of 0.60 c. c. of dihydroxyethylsulphide. No local lesion. No diarrhea.

Time	Temperature (degrees)	Weight, in grams	Notes
Jan. 8, 9.25 p. m.-----	104.6	2, 110	0.60 c. c. of dihydroxyethylsulphide subcutaneously. No evidence of local irritation, and animal eats at once when released.
9, 8.30 a. m.-----	103.2	2, 100	No diarrhea. Very slight edema at site of injection.
2.30 p. m.-----	-----	-----	No diarrhea.
2.45 p. m.-----	-----	-----	Killed with chloroform. Autopsy at once.

Autopsy.—There is a slight congestion of all organs. Stomach is well filled, its mucosa grossly negative. Intestines: Apparently negative. Formed feces in lower colon. No evidence of diarrhea. The bladder contains a very turbid yellowish-white urine. No other changes.

Microscopic findings.—Lung: Slight congestion. No edema. Kidneys: Negative. Slight congestion. Adrenals: Negative. Spleen: Negative. Liver: Marked fatty change. Gall-bladder: Epithelium perfectly preserved. No changes. Small intestine: Slight, but well-defined catarrh. Congestion of mucosa. Excessive mucus formation. Stomach: Negative.

INTRAVENOUS INJECTION OF DICHLORETHYLSULPHIDE

The following condensed protocols are selected from the various series of intravenous injections. In every case in which dichlorethylsulphide was given, it was injected without dilution. Although bland oils will serve as suitable diluents so far as mutual solubility is concerned, the certainty of producing some degree of fatty embolism, with resulting confusion in the pathologic picture, renders this method inadvisable. In addition, the much greater solubility of dichlorethylsulphide in the oil than in the body fluids may be expected to retard its action and delay the production of its characteristic symptomatology.

PROTOCOLS

RABBIT 53.—Intravenous injection of 0.06 c. c. of dichlorethylsulphide. General convulsions. Marked reduction of temperature. Prostration. Death in less than three hours.

Time	Temperature (degrees)	Weight, in grams	Notes
Dec. 9, 2.50 p. m.-----	101.5	1, 570	0.06 c. c. of dichlorethylsulphide given intravenously in superficial femoral vein. Light chloroform anesthesia. Animal made quick recovery from anesthesia, soon moving about.
3.50 p. m.-----	94.0	-----	Animal very much weaker. Respiration very rapid. Easily startled by sudden movements or unexpected noises. Slight convulsive movements. No general convulsion.
3.54 p. m.-----	-----	-----	First general convulsion, consisting of irregular rapid movements. There is some opisthotonos but the head is drawn chiefly to one side.
4.15 p. m.-----	-----	-----	Lies on side. Occasional convulsions.
4.45 p. m.-----	-----	-----	Continues to lie on side. Can not turn over. Jerking movements of forepaws, head, and neck. Salivation and lacrymation. Pupils dilated. Respiration slow and irregular.
5.30 p. m.-----	-----	-----	Death. Much stringy saliva during last 15 minutes.
8 p. m.-----	-----	-----	Autopsy.

Autopsy.—Body nearly cold. Rigor mortis marked. Abdomen moderately distended. No diarrhea. Pleural cavities and pleurae negative. Heart: Moderately dilated, particularly on the right side. Dark fluid blood, clotting tardily. Lungs: Air-containing throughout. Congestion moderate, except posteriorly. Spleen: Negative. Kidneys: Slight congestion. Adrenals: Negative. Liver: Marked congestion. Lobules large. Central zones dark red, outer two-thirds of lobule, grayish-red. Gall-bladder: Well filled with a pale mucoid bile. Stomach: Distended with food. Mucosa shows scattered areas of post-mortem change along greater curvature. Upper small intestines contain a thin yellowish mucoid fluid. Lower small intestine is well filled and there are formed stools in the lower colon.

Microscopic findings.—Central nervous system: Congestion. Heart: Negative. Lungs: Congestion. Atelectasis. No edema. No hemorrhage. Spleen: Marked congestion but no pigment. Adrenals and pancreas: Acute congestion. Stomach: Slight cloudy swelling of parietal cells. Congestion. Intestines: In portion examined the mucosa is well preserved. Congestion of villi. No necrosis. Liver: Moderate congestion. Slight fatty degeneration.

RABBIT 51.—Accidental intravenous injection of dichlorethylsulphide in the course of a deep subcutaneous injection. Total injection 0.12 c. c., of which probably less than 0.06 c. c. entered a small subcutaneous vein. Convulsions. Diarrhea. Death in four hours.

Autopsy.—Body still warm but rigor mortis is present. Soft fecal material from anus. Posterior portion of body is much soiled with feces. Pleural cavities and pleurae: Negative. Heart: Right-sided dilatation. Blood, fluid, clotting slowly. Lungs: Free. Slight congestion. Air-containing throughout. Spleen: Negative. Kidneys: Moderate congestion. Adrenals: Negative. Liver: Moderate congestion. Stomach: Distended with food. The first portion of the small intestine contains a very abundant slightly yellow fluid, which is somewhat mucoid. In the descending colon and rectum there are no formed stools.

Microscopic findings.—Heart: Negative. Lungs: Moderate congestion. No edema. Small patches of atelectasis. Bronchioles dilated. No hemorrhages. Spleen: Moderate congestion with few pigmented cells. Kidneys: Congestion. Intestine: Mucosa well preserved. Stomach: Negative. Liver: Congestion. Slight cloudy swelling.

INTRAVENOUS INJECTION OF HYDROCHLORIC ACID PROTOCOLS.

RABBIT 89.—Intravenous injection of 0.06 c. c. of hydrochloric acid. Animal living on fourth day. No diarrhea. No evidence of general reaction.

Time	Temperature (degrees)	Weight in grams	Notes
Jan. 16, 11.45 a. m.	103.0	1,520	0.06 c. c. of strong hydrochloric acid (diluted to 1.20 c. c. with distilled water) in jugular vein. Apparently well.
1 p. m.			No diarrhea.
Jan. 17.....	102.4	1,710	Do.
18.....	103.4	1,680	No diarrhea. Perfectly well.
20.....	104.6	1,600	Killed. Autopsy at once.
20.....			

Autopsy.—Gross findings all negative, except thrombosis of jugular at site of injection.

Microscopic findings.—All negative, except for thrombophlebitis at site of injection.

INTRAVENOUS INJECTION OF DIHYDROXYETHYLSULPHIDE

RABBIT 87.—Intravenous injection of 0.30 c. c. of dihydroxyethylsulphide. Animal living on the fifth day. No diarrhea. No marked loss of weight.

Time	Temperature (degrees)	Weight in grams	Notes
Jan. 15, 4 p. m.	101.6	2,410	0.30 c. c. of dihydroxyethylsulphide into jugular vein. Light chloroform anesthesia. Animal eating. Apparently well.
7 p. m.			No diarrhea.
Jan. 16.....	103.9	2,350	Do.
17.....	102.6	2,320	Do.
18.....	102.4	2,320	Do.
20.....	102.3	2,350	No diarrhea. Perfectly well.
20.....			Killed. Autopsy at once.

Autopsy.—All gross findings negative.

Microscopic findings.—Negative, except for marked fatty liver.

SUMMARY OF EXPERIMENTAL WORK.

Subcutaneous injections.—When pure dichlorethylsulphide was injected subcutaneously in doses of from 0.015 up to 0.60 c. c. the injections were apparently painless and the animals exhibited no signs of discomfort. Even with the

largest doses the animals resumed feeding as soon as released and gave no evidence of local irritation. At varying periods of time, from one hour to several days, depending in part upon the size of the dose and in part upon the rate of absorption, toxic symptoms appeared, usually in the form of salivation, diarrhea, and marked depression of temperature. At first the respirations were quickened; later they became slow. From the largest doses the animal might die within two hours, without diarrhea, but with a short period of nervous excitement followed by coma and gradual failure of respiration. Doses of from 0.015 to 0.06 c. c. were not necessarily fatal to rabbits, although a certain proportion of the animals receiving such doses did die. Death from these doses occurred from the fourth to the tenth day. Diarrheal symptoms might appear as early as the second day, but in the great majority of cases diarrhea did not appear until the fourth to seventh day. Coincident with the diarrhea there was a marked fall of temperature, which could be as much as seven to eight degrees below normal. If the animal survived the diarrheal period, the temperature might come back nearly to, or quite to, normal, to fall again just before death, if the animal died. During the diarrheal stage the animal rapidly lost weight and this loss of weight continued after the cessation of diarrhea, so that when the animal died it might have lost as much as one-third of its body weight. The diarrheal stools were fluid, mucoid, brown to black, sometimes tarry, and very foul smelling. Accompanying the diarrhea, there was a marked anorexia and great thirst; the animal was quiet, depressed; and both circulation and respiration were slowed. In the animals that recovered, the diarrhea might last for several days, accompanied by a marked lowering of temperature and a general depression. As the stools become normal the temperature rose and the general condition improved until the animal was again apparently perfectly normal.

At the site of the subcutaneous injection there developed a local edema which was usually much less than the edema produced by cutaneous applications. In a certain number of cases there was a marked edema of the belly wall, although the injections were routinely made on the back of the animal, apparently due to the hypostasis of body fluid containing mustard gas, from the seat of the injection. The edematous area at the seat of injection gradually changed into an indurated eschar (figs. 210 and 211) which underwent a slow demarcation from the neighboring living tissue. In some animals injected subcutaneously with the dichlorethylsulphide furnished by the Chemical Warfare Service and living two days or longer, a sulphur-yellow coloration of the tissue at site of injection was noted. Such a coloration was not noticed in any animal injected with the Gomberg preparation.

The gross pathology shown by animals killed or dying at varying periods after subcutaneous injections consisted of a general passive congestion of all organs with occasional minute hemorrhages, emboli, and infarctions. The most specific changes were those found in the gastrointestinal tract in the form of an intense splanchnic congestion and a more or less severe catarrhal enteritis. In practically every instance it was noted that the contents of the gall-bladder consisted of a thin, pale, yellowish, mucoid bile.

The microscopic findings confirmed the gross appearances. No specific changes were found in any organs except the intestines, spleen, and possibly the bile-duets. (Figs. 212 to 221.) These specific changes consisted in a mucoid

degeneration, necrosis, and desquamation of the epithelium of the intestinal mucosa, marked congestion of the whole splanchnic area, with edema and occasional petechial hemorrhages and minute erosions of the mucosa. Degenerative changes were also noted in the epithelium of the bile-ducts, and the post-mortem changes in the mucosa of the gall-bladder and larger bile-ducts appeared to be greatly hastened, and more severe than normal, as though from the presence of some necrosing substance in the bile. A very striking feature of the pathology of many cases of subcutaneous injections of dichlorethylsulphide was the presence in the blood spaces and sinnsoids of the spleen of great numbers of large pigmented phagocytes and hemophages containing altered red blood cells, indicating a greatly increased hemolysis. (Fig. 221.)



FIG. 210.—Rabbit. Eschar resulting from subcutaneous injection of 0.03 c. c. of dichlorethylsulphide, 18 days after injection

The microscopic appearances of the tissues at the site of injection were those of an extensive eschar extending entirely through the skin and fascia, and deep into the muscles with extensive extravasations and infiltrations of leucocytes. The appearances of secondary infection were frequently added to those of the primary lesion. In several instances deposits of lime salts were noted in the necrotic area.

Intravenous injections.—When dichlorethylsulphide was injected directly into the external jugular or superficial femoral veins in doses varying from 0.0075 to 0.18 c. c., the animal showed no signs of pain and returned to eating, but within a short time began to show symptoms of hyperexcitability in the form of very rapid respiration and slight convulsive movements. Within an hour there might be general convulsions and opisthotonos with head turned to one side. The animal quickly became very weak, and tended to lie upon its side

with rapid jerking movements of the legs, as though running. The animal could not turn over. Soft feces were frequently involuntarily discharged. The animal acted as though nauseated and there were slight salivation and lacrymation. The pupils were dilated. The temperature rapidly fell 6° to 8° before death. The convulsions ceased, the pupils contracted, salivation increased, the animal passed into coma, and there was a gradual failure of circulation and respiration, although the respiration ceased some time before the heart stopped beating. Death usually occurred in one to four hours, depending upon the size of the dose. Following the intravenous injection of larger doses, the first convulsive movements might appear in 10 minutes and be followed rapidly by wild clonic convulsions, very much resembling those of rabies.



FIG. 211.—Rabbit. Eschar resulting from subcutaneous injection of 0.06 c. c. of dichlorethylsulphide, 11 days after injection

The gross pathologic changes following intravenous injections of dichlorethylsulphide were dilatation of the heart, particularly on the right side, and marked congestion of the lungs with numerous petechial hemorrhages. All other organs showed congestion with numerous minute hemorrhages. Mucosa of gastrointestinal tract was covered with thick mucus, was congested, and might show minute hemorrhages. The content of the gall-bladder occasionally was a thin and pale bile. No specific changes were found in the brain and cord and no thrombus in the vein at the site of injection.

Microscopic examination confirmed the gross appearances, in that it showed extreme congestion, stasis and hemorrhages in the lungs; congestion of the gastrointestinal tract, with an increased formation of mucus scattered irregularly throughout, not comparable, however, to the changes found in animals injected subcutaneously; and marked general congestion.

Epicrisis.—The introduction of dichlorethylsulphide into the blood stream caused death within a few hours with characteristic symptoms. When injected subcutaneously, with resulting slower absorption into the circulation, death occurred later, from 12 hours to several days, likewise with a characteristic symptomatology. The symptoms could be classed roughly as (1) nervous and (2) intestinal. In the case of large doses, with death occurring within an hour, the nervous symptoms alone might be exhibited, while in the animals living for some time the nervous symptoms were slight and those of the intestinal group predominated. In the correlation of the pathologic findings with the symptomatology, no change was found in the central nervous system offering an adequate explanation for a death dependent entirely upon a lesion of the central nervous system. In the delayed cases (subcutaneous) the intestinal tract

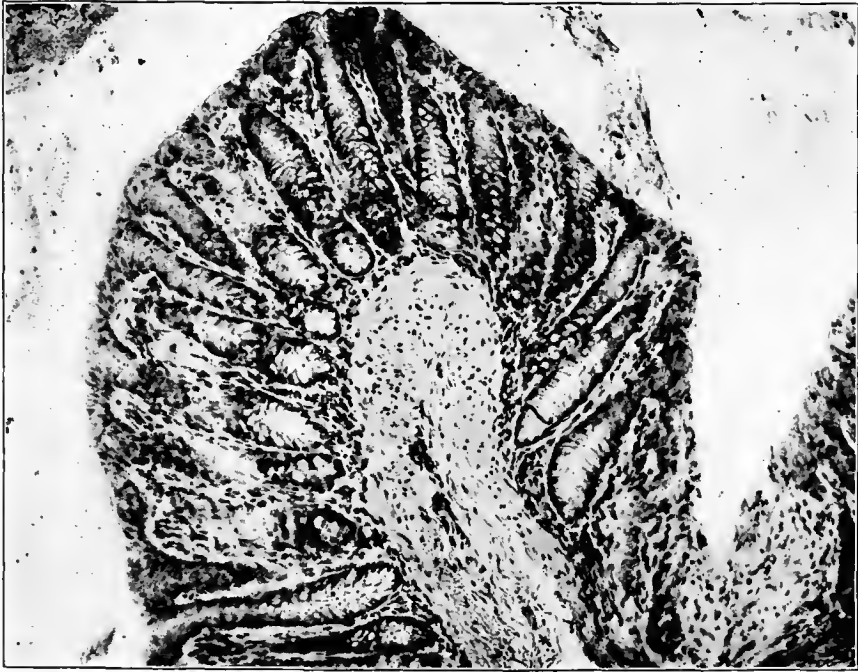


FIG. 212.—Rabbit. Received subcutaneous injection of .045 c. c. of dichlorethylsulphide. Died on third day during mild diarrhea. General mucoid degeneration

offered a pathologic picture commensurate with the symptoms. In addition to the specific pathology just mentioned, incidental pathologic findings in the form of thrombi, emboli, embolic infarctions and hemorrhages could at times be interpreted as explaining some of the observed clinical phenomena.

Of all the pathologic lesions produced by mustard gas, apparently the most specific and most interesting were the intestinal changes following intravenous and subcutaneous injections. The intense catarrhal enteritis observed after such injections suggested the excretion of dichlorethylsulphide or some product of its decomposition through the intestinal mucosa. No changes were observed in the kidneys indicating the excretion of any toxic product through the renal epithelium. In the case of the liver there were observed, at times, degenerative changes in the biliary epithelium, suggesting the presence

of some injurious substance in the bile. Further, the probability of this hypothesis seems the greater in view of certain changes, found in a certain proportion of cases, in the gall-bladder, in the form of an apparently earlier post-mortem necrosis of the gall-bladder wall, and a diffusion of the bile into the neighboring liver tissue. It has been a notable observation that, in many cases, when autopsy was performed immediately upon death of the animal, such early post-mortem change was found in the gall-bladder; while in animals that had not received dichlorethylsulphide injections, such an immediate post-mortem change was not observed.

A large number of experiments were made in the effort to demonstrate the presence of mustard gas or its products in the intestinal wall and contents, and

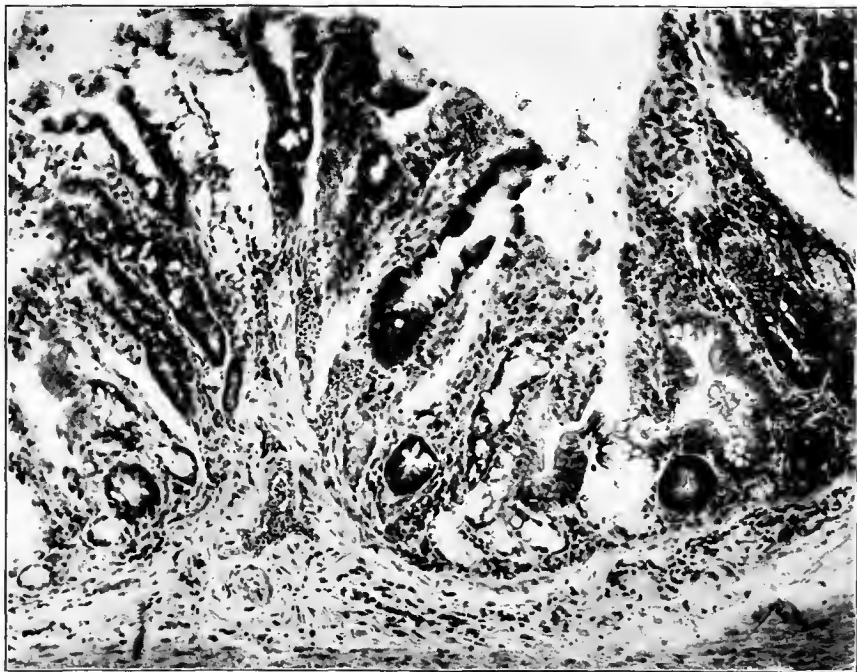


FIG. 213.—Rabbit. Received subcutaneous injection of 0.18 c. c. of dichlorethylsulphide. Began to have diarrhea seven days after injection and died four days later. Section of upper portion of small intestine showing acute catarrhal enteritis

in the liver and bile. In the tissues at the site of the injection, the odor of mustard gas would persist for several days, and cutaneous applications of the ether extract of these tissues produced a well-marked mustard-gas burn, even when the ether extract was much diluted. Further, in one case in which death occurred within one hour after jugular injection, with numerous small embolic hemorrhages in the lungs, the odor of mustard gas was clearly evident on section of the lung, and an ether extract of the lung gave a slight positive test. With this single exception we were unable to obtain any odor of mustard gas or any positive skin reaction from extracts of any organ. Ether and aqueous extracts of the liver and bile, the intestinal tract and its contents, the blood, heart and lungs, and of the urine, even when concentrated, yielded no odor of mustard gas and gave no positive skin test.

It has been generally assumed that the injurious action of mustard gas follows its hydrolysis in the living cells and tissues. The products resulting from the hydrolysis of dichlorethylsulphide are hydrochloric acid and dihydroxyethylsulphide.

From the chemistry department of the University of Michigan a quantity of pure dihydroxyethylsulphide was obtained. Varying series of experiments made with this substance showed it to be apparently inert, both as applied locally, by ingestion, and by subcutaneous and intravenous injections, in quantities up to many times the lethal doses for dichlorethylsulphide. No diarrhea, no fall in temperature, and no other symptoms were produced, and no pathologic lesions were found in such animals with the exception of marked fatty changes in the liver cells.

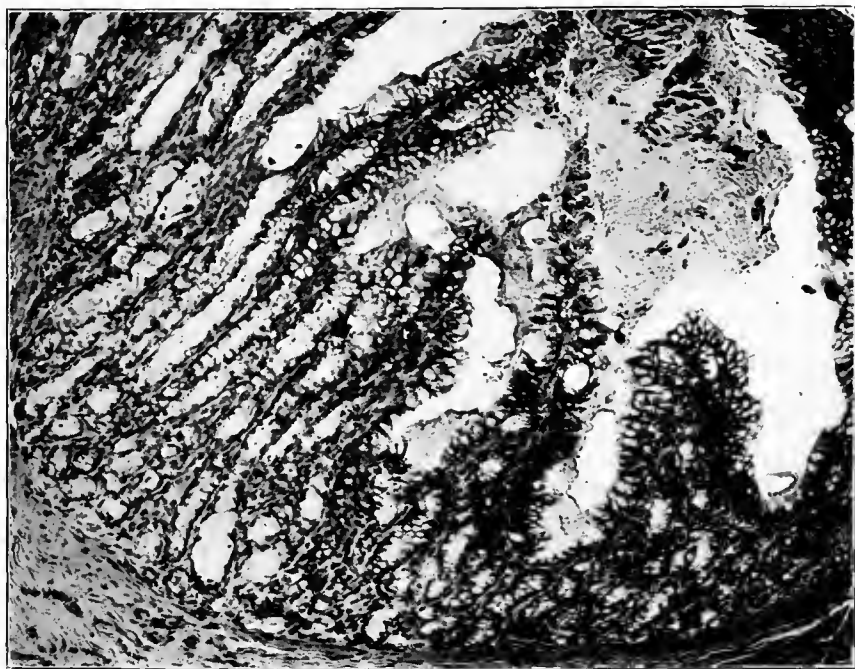


FIG. 214.—Same rabbit as in Figure 213. Extreme mucoid degeneration. Catarrhal enteritis. Mucous diarrhea

A similar set of experiments with hydrochloric acid injections was also carried out. The subcutaneous injection of hydrochloric acid, even in a dose of 0.12 c. c., produced intense local irritation and pain, in striking contrast to the anesthetic action of dichlorethylsulphide. The course of the local lesion was entirely unlike that produced by mustard gas. The liquefaction of the eschar was very rapid and there quickly resulted a deep excavated lesion, the bottom and sides of which appeared charred. (See fig. 222.) No diarrhea was produced; the temperature remained normal or rose; no symptoms were produced, and the animal recovered unless secondary infection set in.

The intravenous injection of 0.06 c. c. of hydrochloric acid (diluted to prevent local injury during injection) produced no symptoms comparable to those resulting from the intravenous injection of dichlorethylsulphide.

The manner of causation of the intestinal lesions remains the special problem of the pathology of dichlorethylsulphide poisoning. Neither hydrochloric acid nor dihydroxyethylsulphide, when introduced into the circulation, will cause similar changes. Therefore these lesions can not be the result of the action of hydrochloric acid produced at the site of the lesion and circulating in the blood. The next most plausible explanation of the cause of the intestinal lesions is that mustard gas itself or some other unknown decomposition product circulates in the blood and is excreted through the mucosa of the intestine, or possibly also through the bile.

It has been stated that the most delicate chemical test for mustard gas is a color reaction with a solution of platinic chloride and sodium iodide. The

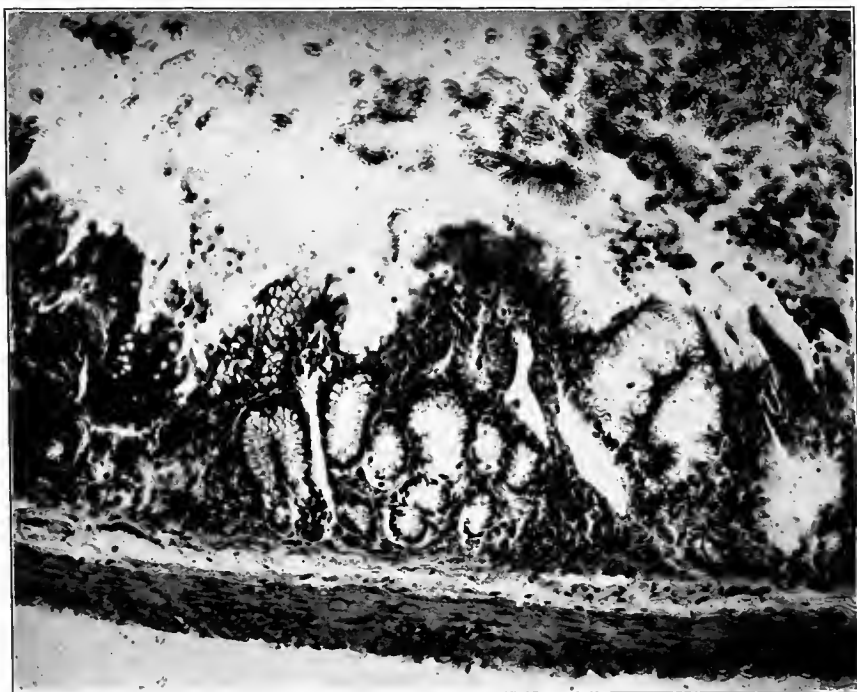


FIG. 215.—Section of cecal wall from same rabbit as in Figure 213. Marked catarrhal inflammation. Mucous diarrhea

liquid to be tested is applied to absorbent paper moistened with this solution. In the presence of dichlorethylsulphide the pink color is changed to a faint purple, which becomes blue or deep blue, depending upon the concentration of the mustard-gas solution. When this test was applied to ether and aqueous extracts of the liver, bile and intestine from animals injected subcutaneously and intravenously with dichlorethylsulphide, a definite blue color was obtained more marked in the case of the aqueous extracts. This reaction at first was believed to be a positive test for mustard gas in these extracts. Continuing the control experiments, it was found that dihydroxyethylsulphide gives the same reaction with the platinic chloride-sodium iodide as dichlorethylsulphide. The aqueous extracts of liver, bile, intestine and urine, which might be expected to have dihydroxyethylsulphide in them, if it were present at all, since it is soluble in water, were then taken and heated with concentrated hydrochloric acid, with

the expectation of reconvertng the hydrolyzed product into mustard gas. The products thus obtained, however, gave no odor of mustard gas, and their ether extracts gave neither a skin reaction nor a positive color test. On the other hand, these aqueous extracts of body fluids and organs did give bluish-green color tests with the test solution that might be interpreted as faint positive reactions for mustard gas. Unfortunately, however, the aqueous extracts of these same organs and fluids from animals untreated with mustard gas produce an identical color reaction. It was impossible, therefore, to demonstrate the presence of mustard gas or its hydrolyzed products in the liver, bile, intestines, feces, blood, or urine.



FIG. 216.—Rabbit. Received subcutaneous injection of 12 c. c. of dichlorethylsulphide. Diarrhea began on second day, the animal dying three days later. Extreme mucoid degeneration of the entire intestinal epithelium. Mucous diarrhea

CONCLUSIONS

1. Dichlorethylsulphide when injected internally in doses of approximately 0.06 c. c. per kilo for the rabbit, and 0.03 c. c. per kilo for the dog, causes a fatal intoxication, characterized, when death occurs quickly, by symptoms referable to the central nervous system; but when death takes place more slowly, by intense diarrhea, anorexia and reduction of temperature.

2. The only specific pathology of such fatal poisonings is a marked degeneration of the epithelium of the gastrointestinal tract in the form of a severe catarrhal enteritis, and the occasional occurrence of similar changes in the epithelium of the bile-ducts and gall-bladder.

3. In a certain number of animals injected subcutaneously a marked hemosiderosis of the spleen was observed. There seemed to be a relationship between the degree of the splenic pigmentation and that of the local extravasations at site of injection. As such splenic pigmentation was not constant, it seems

more likely that it was the result of the local hemolysis and not due to any specific action upon the blood or blood-forming organs. The splenic hemosiderosis also bore a definite relationship to the number of pigmented hemophages seen in the sinuses of the lymph and hemolymph nodes. The latter can be similarly explained. However, since hemosiderosis of the spleen is not an uncommon finding in laboratory rabbits, its occurrence in these animals may have been purely coincident.

4. These changes suggest the excretion of mustard gas or some poisonous product resulting from its decomposition into the gastrointestinal tract. No positive proof, however, of this mode of excretion could be obtained. The hydrolysis of mustard gas circulating in the blood may take place in the intestinal mucosa, thereby producing the degenerative changes seen in these cells.

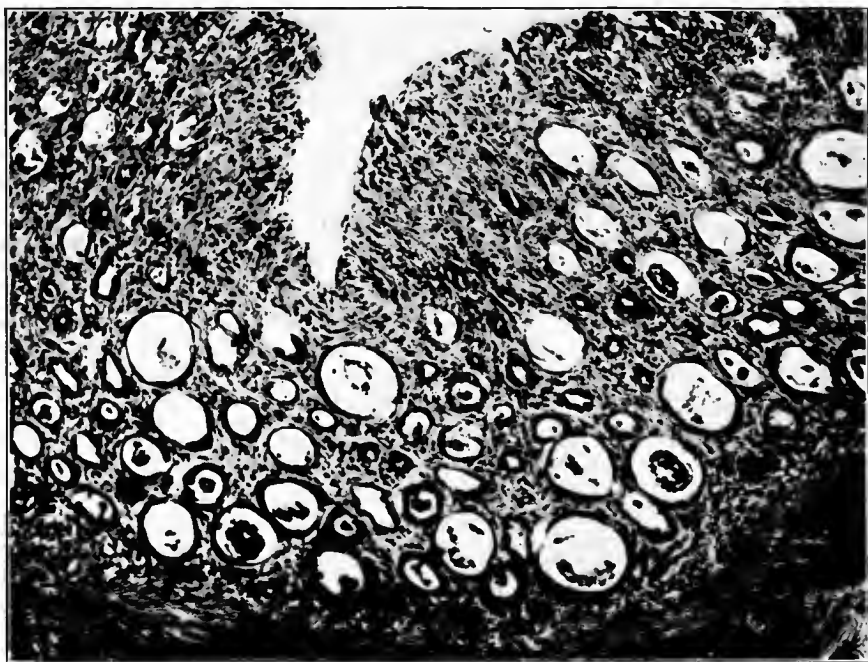


FIG. 217.—Dog. Received subcutaneous injection of 0.24 c. c. of dichlorethylsulphide. Died in four days, with a very severe diarrhea. Extreme catarrhal desquamative enteritis. Mucoid degeneration and necrosis of the glandular epithelium

On the other hand, the intestinal conditions may not be due to the direct action of any substance upon the epithelium of the mucosa, but may be secondary to the splanchnic congestion and the hyperexcitability of the nervous centers.

5. It seems probable that the characteristic symptoms and death following subcutaneous and intravenous injections of dichlorethylsulphide are due to the direct action of this substance circulating in the blood, upon the central nervous system, either with or without hydrolysis in the cells of the nervous tissue affected. As the result of intracellular hydrolysis, hydrochloric acid may be liberated within the cell and give rise to the toxic effects observed. The specific character and constancy of the symptomatology offer sufficient argument against any assumption that the process is embolic in character.

In the series of acutely fatal intravenous injections of dichlorethylsulphide described above, no specific changes in blood or blood-forming organs were noted. Since the appearance of Pappenheimer's preliminary report¹⁰ there was carried out in the pathological laboratory of the University of Michigan a series of investigations using much smaller doses of dichlorethylsulphide in alcoholic solutions. These experiments confirmed Pappenheimer's observation that in rabbits living to the third or fourth day after such injections, there occurs an initial leucocytosis, followed quickly by an extraordinary drop, so that before death the leucocytes may practically vanish from the circulation. Two protocols are given:

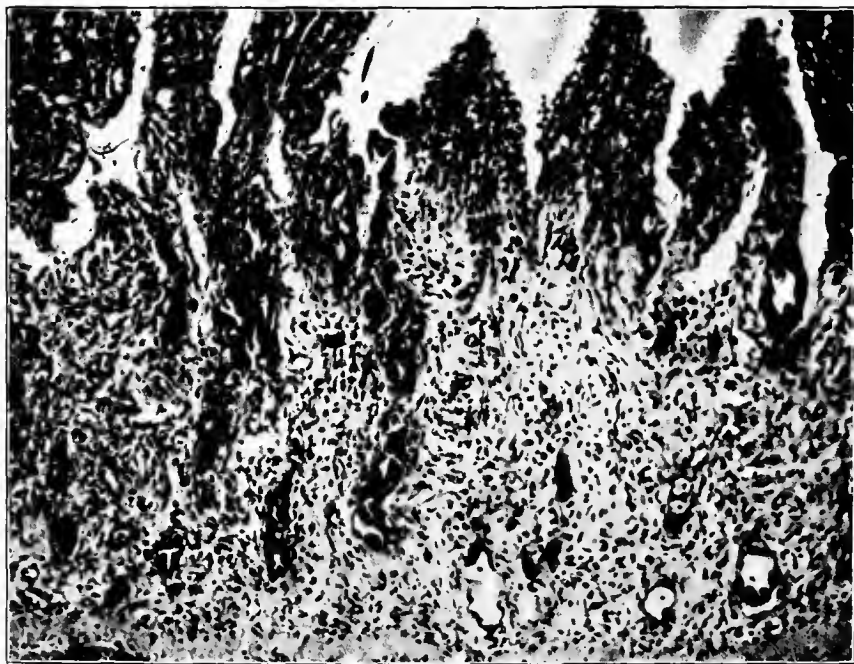


FIG. 218.—Same dog as in Figure 217. Middle portion of small intestine, showing desquamation of the superficial epithelium and necrosis of the epithelium of the gland of Lieberkuehn. Severe enteritis

PROTOCOLS

RABBIT 103.—Injected intravenously with 0.006 c. c. of dichlorethylsulphide in alcoholic solution. A marked leucocytosis was noted in four hours. On the next day the white cells began to fall, and on the third day had reached 275. During this period the red cells remained slightly higher than normal. Blood smears showed only an occasional white cell. These were about equally divided between polynuclear leucocytes and degenerating mononuclears. Died on the fifth day.

RABBIT 104.—Given 0.010 c. c. of dichlorethylsulphide intravenously in alcoholic solution. Showed in 17 hours a leucocytosis of 23,600. On the next day the white cells began to fall rapidly, on the fourth day reaching 325. Smears showed only occasional white cells, about equal numbers of polynuclears and degenerating mononuclears. Died on the fifth day.

Both of these animals showed extraordinary depletion of the bone marrow and, to a lesser degree, of the spleen and lymphoid tissues. The second rabbit showed marked general edema.

Intravenous injections of small amounts of pure dichlorethylsulphide do, therefore, produce a marked leucopenia before death.

SUSCEPTIBILITY

In Meyer's first laboratory experiments with dichlorethylsulphide he noticed an apparent difference in individual susceptibility, in that he, himself, was not affected by exposure to it, while a laboratory worker engaged in making it developed conjunctivitis and a severe skin eruption.¹ Meyer's conclusion that individual susceptibility must vary greatly seems hardly warranted by this observation. Undoubtedly Meyer was working with a very impure compound, the concentration of which must have varied from time to time, and

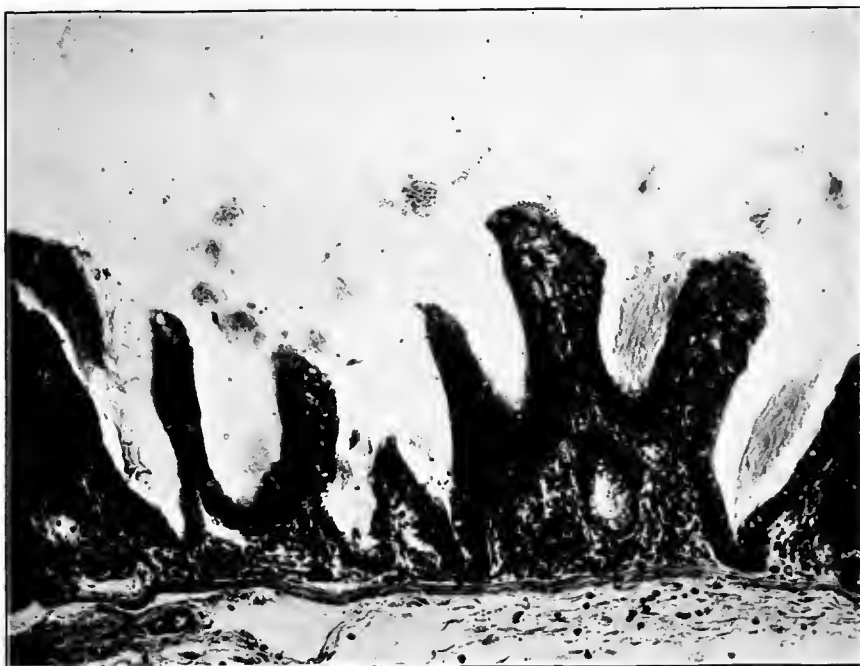


FIG. 219.—Rabbit. Received subcutaneous injection of 0.06 c. c. of dichlorethylsulphide. Very severe diarrhea from fourth to ninth day. Killed 15 days after injection. Mucosa of intestines intensely congested and edemations. Marked mucoid degeneration with cystic glands. Regeneration of superficial epithelium

the laboratory worker must have been much more exposed to its fumes than Meyer himself. Further, the dissemination of mustard gas is such an insidious matter of physical conditions and pure chance, that in a group of workers exposed to apparently identical conditions the greatest diversity of effects may be produced, leading to an incorrect supposition of especial resistance or susceptibility in the individual members of the same group. The question of the existence of individual susceptibility can be settled, therefore, only by the application of experimental methods in which the conditions of exposure are identical.

An acquired hypersensitivity to mustard-gas vapor as the result of previous or repeated burns is claimed by many workers and accepted by some observers.

That such a localized susceptibility may be shown in scars, healing burns, injured conjunctiva and mucous membranes, is very probable, and our own observations bear this out, but there is no evidence to the effect that exposures to mustard gas increase the individual's susceptibility on the part of the whole organism to this substance.

The individual human sensitivity is in part a racial one and, therefore, intrinsic and constitutional. Marshall¹¹ would explain it as due to differences in the skin, cutaneous lipoids, etc. Among the individuals of the same race showing differences in cutaneous sensitivity to mustard gas he noted no other constitutional differences or peculiarities. In the cases seen by us there were five individuals who seemed to be cutaneously hypersensitive, as shown by their

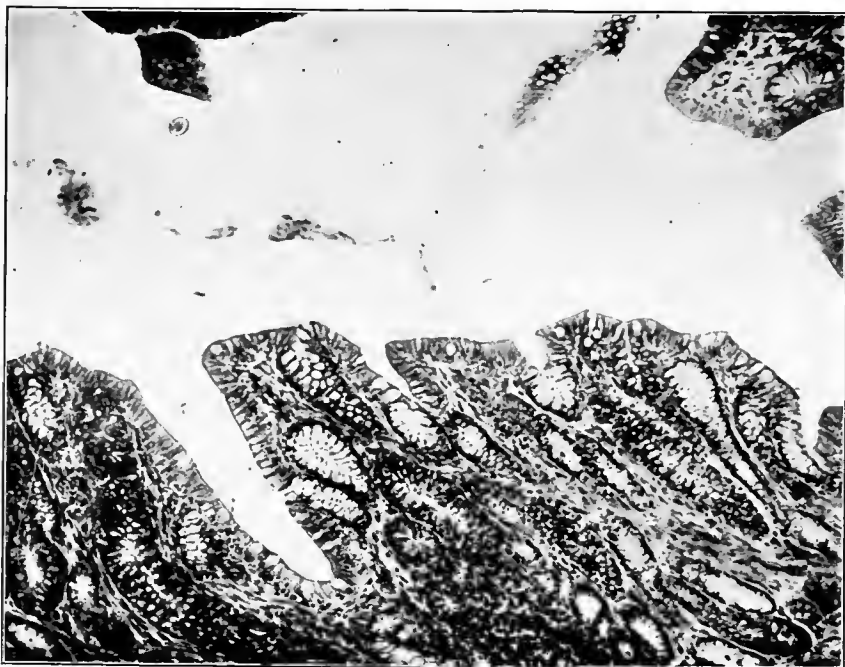


FIG. 220.—Rabbit. Received subcutaneous injection of 0.06 c. c. of dichlorethylsulphide. Very severe diarrhea on fifth to seventh day afterwards. Apparent recovery. Killed on the thirty-second day after injection. Mucosa shows excessive mucous formation

receiving frequent and severe burns from vapor exposures not affecting other workers so severely, although apparently similarly exposed. The two fatal cases belonged to this group. It is noteworthy that all five of these cases presented constitutional stigmata or clinical symptoms of a definite pathologic constitution, the thymicolymphatic.

GENERAL SUMMARY OF DICHLORETHYLSULPHIDE (MUSTARD GAS) POISONING

LOCAL ACTION

Skin.—Dichlorethylsulphide (mustard gas), in liquid or in vapor form even in very low concentrations, is an escharotic poison for the animal tissues (skin, conjunctivae, cornea, mucous membranes of respiratory and gastrointestinal tracts) with which it comes in direct contact. The degree of the injury

is proportionate to the concentration of the gas, the time of exposure, individual susceptibility, and local physical conditions, such as moisture, sweating, warmth, pressure, and friction. The escharotic action, is, for the greater part, painless, the anesthetic effect being especially notable upon the skin; while upon the mucous membranes its action may be more irritant, probably chiefly reflex in character. The cutaneous surfaces most susceptible are those with thinner, more delicate skin, well supplied with sweat glands and hair follicles, where sweat may collect, and which are exposed to friction or pressure, such as the axillae, flexor surfaces, genitals, inner surface of arms and corresponding surface of trunk, inner surfaces of thighs, and between the fingers. There is a penetration of the gas into the sweat and sebaceous glands, and a re-solution

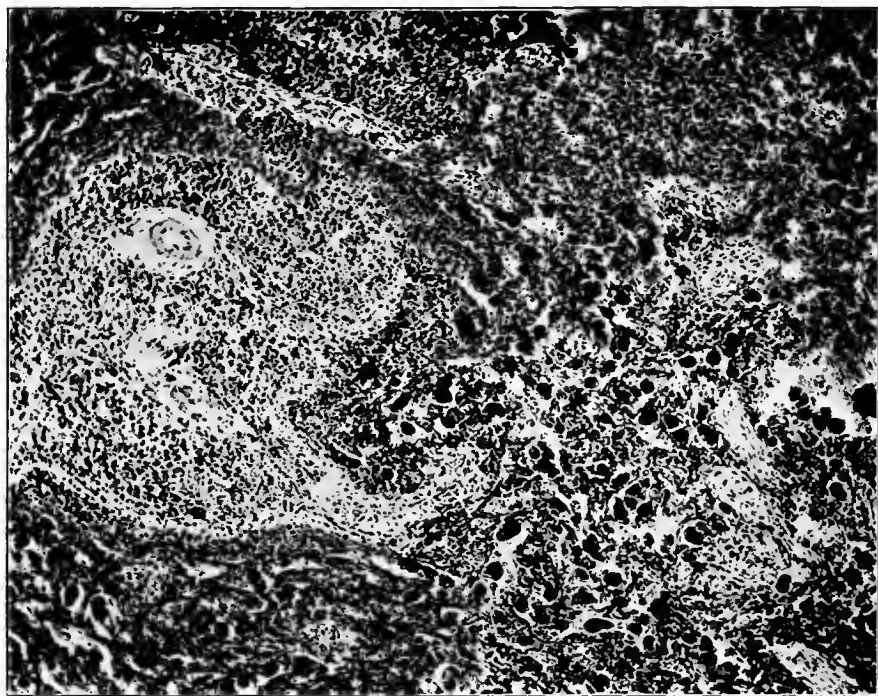


FIG. 221.—Rabbit. Received subcutaneous injection of 0.03 c. c. of dichlorethylsulphide. Very severe diarrhea on fourth to eighth day. Died on twelfth day after injection. Intestines showed severe catarrhal enteritis. Section of spleen showing the great number of pigmented phagocytes in the blood sinuses

of mustard-gas vapor in sweat and sebum occurs. The injuries are particularly striking in their insidious, slowly progressive development, becoming first apparent only some hours after exposure. Upon human skin the lesion appears as a hyperemia, followed by vesication, eschar formation, sloughing, and slow healing, with more or less pigmentation. Depilation may occur; in severe cases the eschar may extend entirely through the corium into the subcutaneous tissues. Secondary infection and gangrene of the eschars occurs invariably in cases not properly treated. Milder lesions may show only the earlier stages of hyperemia, vesication, or pigmentation. In general the injuries may be classed as burns of first, second, or third degree. Following extensive hyperemias in human skin a most marked pigmentation, exceeding in degree the most marked forms of solar tan, may be quickly developed and fade slowly. The pigmentation may

be diffuse or spotted. In human skin vesication is pronounced; in animals the cutaneous lesions are characterized by the development of marked subcutaneous edema in the injured area. The fluid of the vesicle or of the edema is nonirritating when applied to uninjured areas. In the case of human skin frequently exposed to very dilute concentrations (only perceptible by odor), an eczematous itching condition between the fingers, on the genitals, and other parts, may develop; rubbing or scratching of the itching part may lead to the quick development of a blister or superficial eschar (Nikolsky's sign). Such interdigital lesions in laboratory workers may resemble clinically those produced by the itch mite. The genital lesions may be mistaken for venereal sores. Cutaneous areas injured by mustard gas are rendered more susceptible to trauma or



FIG. 222.—Rabbit. Sloughing lesion produced by subcutaneous injection of 0.60 c. c. of hydrochloric acid, 24 hours after injection

other forms of injury, including new exposures to mustard gas. This local susceptibility is, however, a general one, and not a specific lowered resistance to the action of dichlorethylsulphide. Subcutaneous injections of pure dichlorethylsulphide produce painless eschars, followed by dry sloughing with edema less marked than in the case of external cutaneous application; a hypostatic edema may develop on the animal's belly when injected in the back. In the tissues at the site of the injection and in the hypostatic edema mustard gas may be present for some days after the injection as shown by odor and physiologic reaction. The resolution of mild skin injuries is often attended by troublesome itching. Healing of the deep cutaneous eschars is very slow; during the healing of extensive deep lesions the patients complain of a sensation

of "tightness" or contraction of the skin; large scars may be produced resembling those resulting from deep thermal burns. The hairs may be lost; but when regenerated they may be white in color. Mild burns may be more painful than severe ones.

Eye.—Upon the cornea mustard gas exerts an especially injurious action, particularly at the vertex. Within 10 to 15 minutes after exposure to dilute concentrations, degeneration or necrosis of the corneal surface may be demonstrated by the application of a 2 per cent alkaline aqueous solution of fluorescein, the injured cells retaining a greenish fluorescent coloration. In more severe injuries the cornea may be killed throughout its entire thickness at the vertex. The mildest cases show a slight cloudiness; the severe cases present a characteristic porcelain appearance of bluish-white opalescent cloudiness, often with a more opaque band or line running horizontally across the cornea just below its transverse diameter. The injury to the conjunctiva is shown by the development of a more or less severe catarrhal, seropurulent or purulent conjunctivitis with marked edema of the subconjunctival tissues leading often to "ruffling" of the lids, entropion, ectropion, or a combination of these. Even the lighter cases tend to run a chronic course with disturbances and reduction of vision. In the severe cases cicatrization and vascularization of the cornea take place slowly with resulting impairment or loss of vision. The injured eye is more susceptible to infection; and in infected cases suppurative panophthalmitis may develop with complete destruction of the eyeball. Recovered cases of mild mustard-gas conjunctivitis often show an increased sensitivity to the action of light, dust, and other irritants, including mustard-gas fumes.

Respiratory tract.—Upon the mucosa of the respiratory tract mustard-gas vapor produces a local injury to the epithelium as shown by the development of a catarrhal, desquamative, membranous, diphtheritic or purulent inflammation (rhinitis, stomatitis, pharyngitis, laryngitis, tracheitis, and bronchitis), these lesions being most severe in the nose, back of tongue, palate, pharynx, and larynx, decreasing in intensity downward. Coryza, salivation, dryness of mouth and throat, aphonia, and persistent cough are the chief symptoms, with physical signs of laryngeal, tracheal and bronchial involvement, and atelectasis, emphysema, and edema of the lungs. As a result of secondary infection a purulent bronchopneumonia may develop.

Gastrointestinal tract.—Through the swallowing of air, saliva, or secretions from the upper respiratory tract containing mustard gas, or from the ingestion of contaminated food, local corrosive action upon the alimentary mucosa may be produced, varying from a catarrhal inflammation to large areas of eschar formation with resulting gastric ulcer, perforation, etc. The symptomatology of the mildest lesions is covered up by that resulting from the more severe burns elsewhere; the more severe ones will produce marked symptoms referable to the stomach and intestines.

Susceptibility.—There exists a racial (whites more susceptible than negroes) and an individual susceptibility to the action of dichlorethylsulphide, particularly in the case of the skin, and probably also of the respiratory tract. The individual susceptibility, in some cases at least, is associated with the constitutional stigmata and symptomatology of the thymicolymphatic constitution. Acquired susceptibility is not specific. Animals show also generic and individual differences in sensitivity to mustard gas.

Systemic action.—There is no evidence of any systemic poisoning by the absorption of dichlorethylsulphide from the skin, eyes, or mucous membranes of the respiratory or gastrointestinal tracts. There is no metastatic action of the gas from the site of local external application.

Shock.—In all severe cases of mustard-gas burns of skin, eyes, or mucous membranes there is usually the clinical picture of severe shock, in the form of intense pallor, depression of pulse and temperature, general collapse, nausea, and vomiting. The mildest cases show no systemic reaction.

Blood and urine.—No changes are observable in the blood or urine of mild cases. In cases with large infected burns of skin or respiratory tract the blood presents a mild secondary anemia, with leucocytosis; the blood urea is increased; the urine is diminished, concentrated, and contains casts and albuminuria. Under forced fluids the urinary symptoms improve and the blood urea diminishes. In severe infected cases the general picture may be that of a severe toxemia. In experimental animals, after more severe gassing with involvement of the respiratory tract, there occurs a distinct concentration of the blood, with a polycythemia of two to three million above the normal, and a corresponding leucocytosis.

Intravenous and subcutaneous injection.—When injected intravenously or subcutaneously dichlorethylsulphide is an active poison, causing death in one to four hours intravenously and two hours to three weeks after subcutaneous injections (for rabbits intravenous injections of 0.0075 c. c. per kilo may be lethal within four hours), according to size of dose, individual animals, etc. When death takes place quickly the symptoms are chiefly those of an action upon the central nervous system, such as hyperexcitability, rapid respirations, general convulsions, opisthotonos, gradual failure of respiration and circulation, coma, and death. When the animal lives longer after small intravenous injections, or after subcutaneous injection, there develops a characteristic symptomatology of salivation, marked diarrhea, leucopenia, and fall of temperature, with marked anorexia, emaciation, and depression. With subcutaneous injections of 0.015 to 0.06 c. c. death usually takes place from the fourth to the tenth day.

PATHOLOGY

The specific microscopic pathology of the local lesions of dichlorethylsulphide poisoning consists in degeneration and necrosis of the cells with which it comes in contact. The earliest microscopic change is pyknosis of the nucleus and cell body, followed by hydropic degeneration, liquefaction or coagulation necrosis. In the skin, hyperemia, with regeneration of the damaged cells, pigmentation, vesicle formation, desquamation of the dead epidermis or eschar formation mark varying stages of severity of the lesion. The degenerative changes extend deepest in the hair follicles and sweat glands. In mild burns without vesication the papillary layer of the corium may show a greater degree of necrosis than the epidermis itself, thus explaining the frequent occurrence of Nikolsky's sign. Large, heavily pigmented chromatophores may be the only living cells left in the papillary layer. In severe burns the necrosis may extend entirely through the corium. In the cornea, pyknosis and simple or coagulation necrosis of the corneal epithelium and interstitial substance, even to the endothelial layer, in extent varying with the degree of exposure, constitute the microscopic features. On the conjunctivæ the epithelium shows pyknosis, hydropic degeneration, liquefaction necrosis, or there may be a deeper necrosis

extending into the subconjunctival tissues. The conjunctival surface suffers to a less degree proportionately than the epidermis. On the mucous membranes the epithelium shows pycnosis, hydropic or mucoid degeneration, desquamation, liquefaction or coagulation necrosis. The necrosis may extend into the submucosa, but the depth of the lesions on the conjunctivæ and the mucous membranes of the respiratory tract is never so great from identical exposures as it is in the skin. Following the necrosis there is marked hyperemia, and the development of an edema, more marked in the subcutaneous and subconjunctival tissues in animals, but less marked in man. Human skin, however, shows a much greater tendency to vesication. The blood vessels in the necrotic area are killed, the blood cells hemolyzed to some extent without thrombus formation or much extravasation, except minute hemorrhages by diapedesis. Following the lesion there is a demarcating inflammation, with slow regeneration, repair, or cicatrization. The regeneration of the epidermis proceeds from the epithelium of the sweat and sebaceous glands. On the mucous membranes there results in the severe cases a localized eschar or ulcer, or a more diffuse diphtheritis. With secondary infection the inflammatory process becomes purulent or suppurative. The influence of secondary trauma and infection is well shown in the early development of deep areas of decubitus in the injured regions of the skin. Multiple furuncles may develop, or large cutaneous areas become gangrenous. In the eye purulent involvement of the anterior chamber, iris, and ciliary body may occur, or even a suppurative panophthalmitis. In the respiratory tract secondary infection of the injured mucosa may lead to a purulent bronchopneumonia.

The internal organs in animals with mustard-gas lesions of the skin, eyes, respiratory or gastrointestinal tract offer nothing of a specific pathologic nature. There is general congestion, marked splanchnic congestion, acute catarrh of the intestines, and, in infected cases, some cloudy swelling of the kidneys.

In fatal cases the cause of death is to be found in shock, secondary infection with toxemia, or local conditions as laryngitis, tracheitis, bronchitis, and bronchopneumonia. It is also possible that the entrance into the body of shell fragments carrying liquid dichlorethylsulphide might cause a relatively speedy death through absorption.

At the site of subcutaneous injections there is found a local eschar with demarcating hemorrhage, edema and inflammatory infiltration; in the large veins into which injections have been made, no changes have been found except occasional thrombosis.

The general pathology of the injected cases presents a specific pathologic picture in the intestinal tract in the form of a severe mucoid, desquamative or necrotic enteritis, the intestinal epithelium showing the most marked hydropic or mucoid degeneration, even to liquefaction necrosis. Similar changes may be found in the epithelium of the bile-ducts. In a certain number of cases the spleen, lymph nodes, and hemal nodes show a marked hemosiderosis, the hemosiderin being contained in large hemophages. It is most probable that these evidences of increased hemolysis are explainable by the extravasations and blood destruction occurring at the site of the injection, or are simply coincident pathology due to some other cause as such hemosiderosis is not a rare finding in laboratory animals. Marked depletion of the bone marrow is produced by small doses intravenously. In the other organs no pathologic changes but congestion and edema have been found, with the rare exception of emboli or thrombi.

MODE OF ACTION

The cause of death in intravenous and subcutaneous injections would appear to be the direct action of minute quantities of free dichlorethylsulphide, or some poisonous product resulting from its decomposition, upon the cells of the central nervous system. It has been assumed that the pathologic action of dichlorethylsulphide is due to its hydrolysis within the tissue cells. The products of this hydrolysis, hydrochloric acid and dihydroxyethylsulphide, when injected into the blood, do not produce the same effects. Dihydroxyethylsulphide and hydrochloric acid, when injected into the circulation in much larger doses than would result from the hydrolysis of the fatal doses of mustard gas, are harmless. The effect upon the cells of the central nervous system, however, may depend upon hydrolysis, with the liberation of hydrochloric acid (Marshall) in these cells, of minute quantities of mustard gas from the circulation, or these cells may be injured without such hydrolysis occurring. It is probable that the gastrointestinal catarrh resulting from the injections of dichlorethylsulphide is secondary to the nervous injury, rather than to an excretion of the poison or poisonous products through this tract, although this point remains unsettled. No positive tests for dichlorethylsulphide or dihydroxyethylsulphide have been obtained in the bile, intestinal contents, or urine. Investigations, therefore, failed to confirm Marshall's statement that dihydroxyethylsulphide is excreted in the urine in mustard gas poisoning. Incidentally, it has been shown that the platonic chloride-sodium iodide color test for dichlorethylsulphide is not applicable to the body fluids or extracts of various organs and tissues, as similar color changes are produced by some of these.

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CHAPTER XVI

THE COMPARATIVE SKIN IRRITANT PROPERTIES OF MUSTARD GAS AND OTHER AGENTS^a

The extensive use of chemical substances in gas warfare led to a systematic study of compounds which irritate the skin. The various compounds submitted by the chemical offense section of the Chemical Warfare Service were compared with dichlorethylsulphide (mustard gas), imitating field conditions in warfare as closely as possible; that is, the skin irritant efficiency of the new compound as compared with dichlorethylsulphide was determined. A brief summary of the methods used and results obtained is here presented. This may be of interest in toxicology and pharmacology, particularly since it is believed that about one-half of the 70 compounds studied have not been previously described.

METHODS

DIRECT APPLICATION

This was made use of principally in chronic experiments with various animals. The method was devised by Lynch¹ at the American University. A 5 sq. cm. area of skin suitably prepared (by shaving and washing) was selected and to this was applied 0.005 c. c. (from a pipette graduated to deliver 0.005 to 0.05 c. c.), or 5 mgm., of the compound, equivalent to the application of 0.001 c. c. (or 1 mgm.) per square centimeter of skin. No precaution was taken to confine the vapors of volatile compounds. The time of appearance of hyperemia and other changes was noted, and the extension and severity of all changes was studied quantitatively as much as possible from day to day and the results expressed in terms of square centimeters of area involved. Dichlorethylsulphide was chosen as the standard by which the irritant properties of other compounds were judged.

On human skin the tests were made by touching a small area with a fine glass rod dipped into the irritant. This method could not be used quantitatively.

VAPOR

Preliminary tests with vapors of volatile compounds were made by two methods devised by Lynch.² One method consisted of placing a small excess of the compound on a plug of cotton in a test tube of 1 cm. diameter and 5 cm. from the opening of the tube. This was allowed to stand long enough to secure a saturation of the column of atmosphere in the tube and then the tube was applied for variable lengths of time to the skin.

The other method consisted of placing a small excess of the compound on a plug of cotton in the bottom of a test tube (1 cm. diameter and about 10 cm. long) which was inclosed in a water jacket made from a long test tube (20 by 180 cm.). The tube was stoppered and allowed to stand for one hour at about

^a These investigations were conducted by the dermatological unit, section of pharmacology and toxicology, Chemical Warfare Service, American University Experiment Station, Washington, D. C. They were reported in *The Journal of Pharmacology and Experimental Therapeutics*, Baltimore, Md., 1919, xiv, 228.

25° C. before exposure to the skin was made. The vapor concentration in both methods was unknown, although in the latter it was practically saturated. For quantitative purposes the following method was used and in connection with it a special skin applicator was devised.

QUANTITATIVE VAPOR METHOD³

This consisted of blowing air by means of an ordinary motor blower through concentrated sulphuric acid and calcium chloride, then through a bubbler containing the compound, and connected with a series of glass skin applicators by means of glass tubing as much as possible. The skin applicator consisted of a small glass cylinder of about 1.5 to 2 cm. in diameter and about 4 cm. long with a small glass handle attached on top, two small tubes at opposite ends for the passage of air laden with the vapors of the compound, and an opening on the bottom for the exposure of skin to the vapor. This opening was 1 cm. in diameter and remained closed until it was established that the vapors were of constant concentration. When the concentration of vapor was constant, the exposure to the skin was made directly for any desired length of time.

The concentration of vapor was determined by dividing the loss of weight of the compound in the bubbler by the total volume of air which was passed through as indicated by the flowmeter. The concentration (nominal) was expressed in terms of milligrams per liter. With certain compounds, the nominal concentrations agreed within 10 to 20 per cent by chemical analysis, and this was satisfactory enough for our purposes. The skin irritant efficiency for the vapors of different compounds was judged by comparison of the lowest effective concentrations and the per cent of positive responses to approximately equal concentrations of the vapors, using dichlorethylsulphide as standard.

USE OF COMPOUNDS IN SOLUTION

The compounds were dissolved in suitable solvents, such as absolute alcohol, liquid petrolatum, olive oil, benzene, carbon tetrachloride, and chlorbenzol, for the purpose of determining the lowest effective concentrations, and for the determination of their skin irritant efficiencies, using two or three solutions which were not effective to four or five which showed positive effects. A definite quantity, usually about 0.02 c. c., was applied to a definite area (1 sq. cm.) of human skin. Larger quantities—that is, about 0.1 c. c. per 5 sq. cm. of skin—were used on dog's skin, so that the concentration per square centimeter of skin was exactly the same for the different species.

However, it was found that so far as the determination of skin irritant efficiency for the purposes of the experiments was concerned the use of the compound in different solvents was not always satisfactory. With certain compounds the skin irritant efficiency determined in this way did not agree with those determined by direct application and the different vapor concentrations. This is attributed to differences in volatility, lipoid solubility, coefficient of solubility of compound in skin and solvent, and formation of insoluble and decomposition products. Under the conditions these factors could not be adequately investigated.

SELECTION OF SPECIES

Dogs were used principally, owing to the limited amount of human material and the large number of compounds studied. Human skin was used as much as permissible and possible. Monkeys, a horse, and the cock's comb and wattles

were also used. The skin of monkeys responded in the same way as that of dogs. The cock's comb responded principally by local inflammation and necrosis.

So far as known the skin of animals does not blister. Mild effects of irritants on the skin of animals are indicated by simple hyperemia, rashes, moderate swelling and edema, also moderate petechial hemorrhages. Instead of vesication, the more severe effects are characterized by rather extensive edema and swelling, and the severest effects by gangrene and ulceration.

On the other hand, the acute and more severe effects on human skin are characterized by hyperemia and vesication, sometimes pustulation, and the severest effects also by ulceration. The scars in the skins of different species do not differ greatly, and depend upon the degree of ulceration and extent of destruction of tissue. The skin of the Mexican or African hairless dog is said to respond to the action of such irritants as cantharides in the same way as human skin, but this was not tried. The part played by the sudoriporous and sebaceous glands in the entry (absorption) of the compounds into the skin was also not studied. In this connection it is interesting to note that horse's skin, which contains sweat glands, was found to be more sensitive to a number of the compounds than the skin of men, dogs, and monkeys. This observation is confirmative of the French.⁴

Rodents were not used in this work, but the results obtained by others indicate that their response to the various irritants is about the same as that of dog's skin.

No marked differences between shaved and unshaved skin of men were observed, greater susceptibility in animals perhaps being in favor of shaved skin. Great individual variability in both human and animal skins was encountered. It appears that repeated exposure of human skin renders it sensitive and eventually unreliable for further experimentation, although the original lesions may be completely healed. As a rule, pigmentation of skin tended to protect against the irritation by the different compounds. This was frequently tested out in animals by exposing a portion of a large freckle or pigmented spot with neighboring white skin in animals simultaneously to the irritants (vapors and liquid), and almost invariably the pigmented area escaped from the effects entirely. It was suggested by Sollman⁵ and observed by Marshall⁶ at American University, that the skin of negroes was more resistant than the skin of whites to irritant effects of dichlorethylsulphide.

SUMMARY

The following brief summary compiled from a large number of results may be presented at this time:

1. The following compounds were found to be severe irritants as indicated by hyperemia, swelling and edema, ulceration, necrosis, etc., on dog's skin and similar changes, together with vesication on human skin: Arsenic trichloride, bromine trifluoride, chlorisonitrosoacetone, dinitrochlorbenzol (parazol), ethyldichlorarsine, dichlorethylsulphide (mustard gas), iodine pentafluoride, methyldichlorarsine, methyl and propyl "mustard" mixture, methyldibromarsine, phenyldichlorarsine, selenium bromine ethylene derivative, dichloro-diethylselenide, "mustard" titanium tetrachloride and di-isothiocyanatodimethylether.

2. The following compounds were found to be mild irritants as indicated by simple hyperemia without vesication, mild urticarial rash; moderate swelling and edema and very little or no necrosis: Normal butyldichlorarsine, O-chlorchloracetanilide, chloracetophenone, oil from chloracetophenone, chlorethylmethylsulphide, Costa Rica tree sap,^b dimethylarsinecyanide, diphenylchlorarsine, diphenylcyanarsine, dichlordiethyltellinochloride, dichlordimethyldithioloxalate, iodoacetophenone, isothiocyanmethylether, isothiocyandimethylether, monochlorethylacetate, monobromomethylacetate, selenium chlorine ethylene derivative, selenium ethylene bromine compound, selenium acetylene chlorine compound, dichlordivinyl selenide, trichlordiethylselenide, selenium "mustard," trimethylthioarsenite, trimethylarsenite and chlorphenarsazene.

3. The following compounds produced no objective or subjective effects on human and dog's skin: Ammonia silicon tetrafluoride, bromacetanide, benzyl sulfoeyanate, ethyl ester of fluorsulphonic acid, "mustard"—mercuric chloride product, juglon, lead tetra-methyl, lead tetraphenyl, mercury dimethyl, methyl "mustard," parabromchloracetophenone, tetrachlordinitroethane and mercury trichlorethylene.

4. As a rule the active arsenicals acted more severely than dichlorethylsulphide during the acute stages. The lesions were more painful, indurated and attached. The ulcers were sharply punched out, clean, and dry, and possessed red bases. Healing occurred promptly. The differences between the different arsenicals were principally quantitative.

5. Dichlorethylsulphide acted more slowly than the arsenicals. The acute effects were less pronounced, and it was more chronic. There was less destruction of tissue in the beginning. Swelling and edema were marked, pouchy and soft in animals. The ulcers were irregular, dirty, purulent and foul. The lesions were generally painless, and secondary infection was common. Healing was slow.

6. As judged by the clinical effects in chronic experiments, lowest effective concentrations of the compounds in solution, and in vapor form, the skin irritant efficiency of the more important severe irritants was about as follows in descending order of efficiency: Dichlorethylsulphide ("mustard gas"), phenyldichlorarsine and methylchlorarsine. By direct application, dibromarsine and selenium compounds come next in order.

7. The order of protein precipitant power of some of the arsenicals tested agrees in the same direction with their skin irritant efficiency, and it was possible to correlate this in a general way with the quality of skin lesions produced. On the other hand, dichlorethylsulphide (mustard gas) was the most efficient skin irritant, and its power to precipitate protein was almost negligible, indicating a difference in mechanism of action.

8. Regarding pigmentation of the skin after healing of lesions of several different compounds, the following characteristic features were encountered:

Absence of pigment—dichlordinitrosoacetone.

Faint brown pigment—dichlorethylsulphide.

Deep brown pigment—arsenicals.

Metallic gray pigment—organic selenides.

9. These and other differences in the behavior of a number of the compounds that were noted indicate differences in mechanism of action dependent

^b Composition unknown.

on differences in chemical structure and composition of the irritants and various physical-chemical and physiological factors. These offer possibilities for further elucidation and correlation of the relations between chemical structure and pharmacological action.

Other possibilities worthy of consideration are the uses of these compounds in the production of experimental lesions and in therapeutics (arsenicals in syphilis, etc.).

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CHAPTER XVII

THE INFLUENCE OF SOLVENTS, ADSORBENTS, AND CHEMICAL ANTIDOTES ON THE SEVERITY OF HUMAN SKIN LESIONS CAUSED BY MUSTARD GAS ^a

NORMAL COURSE OF LESIONS

The following sketch of the course of the main clinical phenomena of dichlorethylsulphide lesions is given to serve as a "normal" for judging the modifications produced by experimental measures. Further details of the skin phenomena are contained in Chapter XVI.

Dichlorethylsulphide, as is now generally known, is a very powerful and peculiar irritant. It produces successively simple erythema, cutaneous edema, extensive vesication with coagulated contents, ulceration, and superficial sloughing. The effects, although severe, do not extend beyond the skin or mucous membranes.

Very small doses are effective. The substance is very rapidly absorbed and fixed in the skin. Solvents prevent the effects only if they are applied almost immediately after contact; they are practically useless after ten or fifteen minutes.

On the other hand, the effects develop quite slowly. In the human skin they become perceptible only after from one hour to two days, according to the dosage. Histologic changes, however, start much earlier, probably soon after the entrance of the poison.

With severe burns the destructive effects grow worse for several days. In any case the healing is a very slow process, very much slower than with ordinary burns. Even when healed the burned skin remains abnormal at least for months.

Another striking peculiarity is the entire absence of pain or sensitiveness during the first two days. At this time even extensive blisters cause absolutely no discomfort. This is not due to a true anesthesia, for the sensitiveness to touch is unimpaired. Apparently, the nerves are in some way protected against the poison. A little later (on the third to fifth day), when the necrotic changes develop and the epidermis is more or less destroyed, the lesions become exquisitely sensitive to mechanical and chemical irritation. In milder cases the edema of the skin leads to intolerable itching.

The hypersensitivity increases until the lesion has reached its acme—between 5 to 13 days, according to the severity. During this time the wound tends to become covered by a sloughing pseudomembrane. This condition persists for about a week.

The turn toward improvement generally sets in rather abruptly between the seventh and nineteenth day, so that within two or three days the wound

^a These investigations, which were undertaken in collaboration with the Medical Advisory Board of the Chemical Warfare Service, were carried out in the pharmacological laboratory of the Medical School of Western Reserve University, Cleveland, Ohio. They were reported in the *Journal of Pharmacology and Experimental Therapeutics*, Baltimore, Md., 1918, xi, No. 3, 229, and 1919, xii, 303.

presents a healthy looking granulating surface and the hypersensitiveness is practically gone. This spontaneous change must be taken into consideration in judging the success of methods of treatment.

From here on improvement is steady, but slow and tedious, and likely to be somewhat complicated by furunculosis.

Table 63 gives the average time relations of the experimental burns. They also hold good for clinical burns.

METHODS OF EXPERIMENTATION

The investigation upon the results of which this section is based had the purpose of studying the conditions that might affect the penetration and the toxicity of the dichlorethylsulphide.

Experiments on animals were abandoned after a few trials, since their skin did not react in the same manner as human skin and the effects that did occur were not easily graded.

TABLE 63.—*Mean course of experimental lesions*

	Severity of burn	Number of experiments in group	Rubefaction			Swelling			Itching		Vesication			Painful ulceration			
			First perceived	Full size	Practically gone	Present	Subsiding	Practically gone	Present	Practically gone	Starts	Maximum	Ruptured, shriveled	Pain starts	Maximum	Painless, healing	Healing, practically stationary
Rubefaction without notable swelling (generally vapor burns).	Light ¹	6	1 d.	2 d.													
	Severe	5	3 h.	4 h.	3 d.												
Erythema and swelling	Light	6	12 h.	18 h.		1 d.		8 d.									10 d.
	Severe	9	1½ h.	4 h.	2 d.	1 d.	2 d.	1 w.	12 h.	13 d.							2½ w.
Vesication	Light	9	1½ h.	1½ h.		1 d.			1 d.		2 d.	3 d.	5 d.	3 d.	5 d.	7 d.	4½ w.
	Severe	7	1½ h.	1½ h.		1 d.					1 d.	1½ d.	2½ d.	3 d.	10 d.	17 d.	5½ w.
Ulceration with superficial gangrene		7	1½ h.	1½ h.		1 d.			1 d.		1 d.	2 d.	3 d.	3 d.	10 d.	15 d.	5 w.
Gangrene of entire thickness of skin ¹		6	1½ h.	1½ h.		1½ d.			18 h.						13 d.	19 d.	7 w.

¹ Four hours, livid, white wheals. Eighteen hours, they are surrounded by vesicles. Fourteen to nineteen days the burned skin sloughs off in mass.

The urgency of the problem at the time appeared to justify direct experimentation on human subject.^b Six students volunteered for what were often quite painful experiments. Other experiments were made on the author of this chapter.

APPLICATION

The poison was applied in the form of liquid and vapor. The vapor tests were preferred whenever possible, since the results are very uniform and milder.

VAPOR TEST

In a 1-dram homeopathic vial (about 5 cm. long and 8 mm. internal diameter) was placed a very small piece of cotton wool. On this was dropped 0.01 c. c. of the poison, then another small piece of cotton, carefully wiping the mouth of the vial. This was packed down with a glass rod, and the vial left corked for an hour to one day.

^b W. P. Bowser, W. D. Cassel, S. J. A. Foerstner, S. H. Lesinger, H. H. Loucks, N. C. Wetzel.

In applying, the open vial was held firmly against the skin by the thumb and forefinger for five minutes. The very uniform results on blank tests, and marked difference in the presence of efficient protectives, showed that a more complicated technique was not necessary.

The normal reaction was an erythematous papule that did not go on to vesication.

ALCOHOL SOLUTION

Dichlorethylsulphide, 0.1 c. c., was diluted with 20 c. c. of alcohol (the solution must be used within an hour, as it hydrolyzes fairly rapidly). Of this dilution 0.005 c. c. was blown from a pipette onto the skin and spread with the point of the pipette over an area of about one-half inch diameter. Air was then blown through the pipette over the area, thus evaporating the alcohol, and leaving a thin film of the poison.

The normal reaction of this dosage was a distinct vesicle which healed slowly. This was generally a disadvantage of the method, since it limited the number of experiments that could be made on a subject. It was also difficult to spread the liquid evenly over a painted or powdered skin area.

At first stronger doses were used (0.01 c. c. of 1 per cent), but these sometimes gave rise to excessive reactions.

FILTER-PAPER TEST

In this, 0.1 c. c. of dichlorethylsulphide was spread on filter paper so as make an even stain, about 1 by 5 cm. This was then cut into 10 squares of 5 mm. each, so that each square represented about 0.001 c. c. of dichlorethylsulphide. These were laid on the skin and kept in place by a bandage for one or two hours.

The reaction was altogether too severe, and this method was tried only in connection with fairly efficient protectives.

The lesions were inspected at suitable intervals and frequently photographed.

EFFECTS OF SOLVENTS

The first line of experimentation concerned the effects of water and oil. Dichlorethylsulphide is readily soluble in oil, and very little soluble in water. It therefore seemed probable that these solvents would affect its penetration and the irritation in the same way as they do phenol or true mustard oil. For these it was found that the irritant distributes itself between the solvent and the skin, according to its partition coefficient; the greater its affinity for the solvent the slower will be its penetration into the tissues, and the smaller the irritation, and vice versa.

The results and experiments showed that the same principles apply to dichlorethylsulphide. Water increases the irritation (Fig. 223) and oils render it less irritant (Fig. 224).

Unfortunately, however, the absorption is still very rapid, even in the presence of oils, and the ultimate injury is not very much reduced. The importance of the delayed absorption is further minimized by the fact that the irritation is proportional to the absolute quantity rather than to the concentration of the poison. This difference from most other irritants is explainable on the

assumption that the toxic effects are not due to the dichlorethylsulphide itself, but to its intracellular decomposition, resulting in the liberation of hydrochloric acid within the cells. The degree of this intracellular acidosis would, of course, depend upon the absolute quantity of the dichlorethylsulphide that had penetrated into the cell. Since the poison probably does not leave the cells after its absorption, the *rate* of absorption would have little effect on the absolute quantity absorbed.

Notwithstanding these restrictions, however, the influence of the solvents is quite distinct, within certain limits. The protection by oils is especially efficient in prolonging the time during which removal treatment remains effective. (Fig. 225.)

The efficiency also increases with the thickness of the oily layer on the skin; and this depends largely on the stiffness of the oil or ointment. The efficiency is therefore increased by the addition of powders or "fillers."



FIG. 223.—Detrimental effects of water (vapor tests). Dichlorethylsulphide vapor was applied to the skin; 62, bare skin; 63, skin coated with water; 64, skin coated with sodium bicarbonate water paste; 65, skin coated with soap; 66, skin coated with kaolin water paste. The photograph was taken 7 days after the application. Note the lesion is greatest on the moistened skin (63), as compared with the bare skin (62). Kaolin restrains this somewhat (66). Sodium bicarbonate paste (64) is useless. Soap paste (65) is fairly efficient. (The figures in parentheses refer to experiments)

This effect appears to be purely mechanical, for no material differences exist between the various substances that were tried.

There are, however, differences between the oils themselves that are not explainable on a physical and mechanical basis, and must therefore presumably be chemical. Linseed oil, raw as well as boiled, and codliver oil furnish considerably more protection than do other oils. (Fig. 226.) This is perhaps due to unsaturated fatty acids. The efficiency, however, is also limited. (Fig. 227.)

Under certain conditions, the fats apparently may increase the toxicity; namely, when they facilitate the contact with the poison. This occurs, for instance, when cloth saturated with the oil is laid loosely on the skin. (See fig. 224.)

The following gives a more detailed outline of the experiments and results:

WATER

The effects of dichlorethylsulphide are more severe in the presence of moisture on the skin. This is shown very convincingly by the vapor test, in experiment No. 63. (See fig. 223.)

This action of water is reflected in the attempt to use protective substances as watery solutions or pastes. These are uniformly less effective than the dry substances, and in nearly all cases they are also less effective than the oily solutions or pastes.

Because of their water content, the following rendered the skin hyper-susceptible, so that the lesions were more severe than on the bare skin: 50 per cent glycerin (experiment No. 15); sodium bicarbonate-water paste (experiment No. 64); kaolin-water paste (experiment No. 66); fuller's earth-water paste (experiment No. 68).

The deleterious effects of moistening the skin do not contradict the beneficial effects of washing and scrubbing the skin, after exposure, with soapy solution.



FIG. 224.—Protective action of petrolatum when dichlorethylsulphide is applied as "splash," and when applied through fabric. In experiments No. 10 and No. 11, the alcoholic dichlorethylsulphide was applied directly to the skin; No. 11 was previously vaselined. The protective value of the petrolatum in No. 11 is apparent. In No. 12 and No. 13 the alcoholic dichlorethylsulphide was dropped on a small square of cloth and this was applied to the skin; No. 13 was first oiled with petrolatum. Note that the two lesions are practically alike. The photograph was taken 19 days after the application.

On the other hand, it is evident that the skin should be protected against moisture during exposure by keeping it covered with absorbent dusting powders; or better, by keeping it oiled, if that is practical.

SIMPLE OILS AND FATS

All oils restrain the effects of dichlorethylsulphide. They differ quantitatively, however.

The relative protective efficiency can be seen when the vapor or alcoholic solutions are applied to the oiled skin; but they are especially striking if equal doses of a 3 per cent solution of dichlorethylsulphide in various oils is applied to the skin. The protective efficiency in the different series is in the following order, the most effective protection being at the top, the least effective at the bottom of the list.

VAPOR TESTS^c

(Sollmann)

Boiled linseed oil (53).

Liquid petrolatum (47).

(Loucks)

Castor oil (90).

^c The numbers in parentheses refer to experiments.

LIQUID DICHLORETHYLSULPHIDE APPLIED TO OILED SKIN ^d

(Small dose)

(Large doses)

Petrolatum (11).

Raw linseed oil (117).

Liquid petrolatum (2, 6, 7).

Solid paraffin (122).

Olive oil (3).

Lanolin (4).

DICHLORETHYLSULPHIDE DISSOLVED IN OILS (3 PER CENT)

Raw and boiled linseed oil (111 and 112).

Olive oil (113).

Cod-liver oil (115).

Castor oil (114).

Liquid petrolatum (110).

(See Fig. 226.)

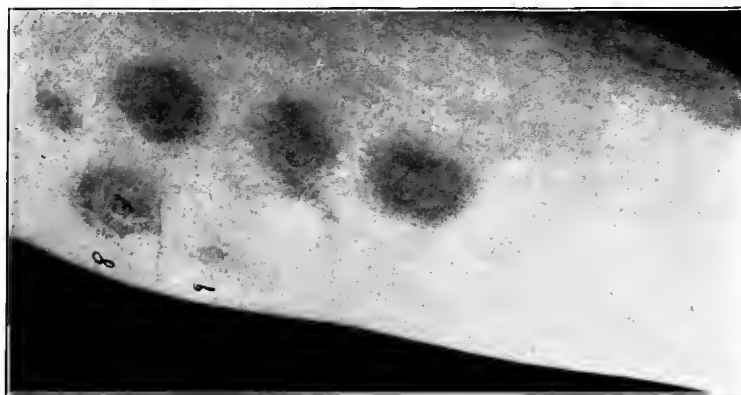


FIG. 225.—Value of protective oiling. In No. 8 the dichlorethylsulphide was applied to the hare skin, in No. 9 to oiled skin. Both were washed with oil after 15 minutes. Observe the much greater effect on the unprotected skin in No. 8. The photograph was taken 24 days after the application

From these data the general order of efficiency is: Linseed oil, raw or boiled, cod-liver oil, solid paraffin, petrolatum, liquid petrolatum, olive oil, castor oil, lanolin.

The oiling of the skin is decidedly protective against slight exposure (experiments 47, 53, 90) to the vapor and fairly effective against small doses of the liquid (2, 3, 4, 11). Its usefulness, however, is not unlimited. Even the most effective oils do not prevent blisters if the strong dichlorethylsulphide is left in prolonged contact (117 to 122). (See fig. 227.)

FILLED OINTMENTS

Many of the substances that were tried as chemical antidotes really acted merely as fillers. The tabulations are again arranged in the order of efficiency, those giving the most complete protection are at the top; the least protection at the bottom. Some of the plain oil are given in brackets for comparison.

VAPOR TEST (SOLLMANN)

Zinc oleate (50).

Liquid petrolatum stiffened with charcoal (50), kaolin (49), or fuller's earth (48).

Linseed oil (53).

^d The numbers in parentheses refer to experiments.

VAPOR TEST (CASSEL)

Zinc oleate (97) and solid petrolatum pastes made with:

Collargol (94).

Zinc stearate (95).

Zinc oxide (96).

Manganese dioxide (98).

Silver abietate (resinate) (101).

Boric acid (99).

Solid petrolatum (100).

LIQUID ALCOHOLIC DICHLORETHYLSULPHIDE

Zinc in liquid petrolatum (21).

Hexamethylamin in liquid petrolatum (20), (petrolatum, 11).

When the dichlorethylsulphide is concentrated, even the filled ointments have only slight values. This is shown by the series 116 to 122, which also includes solid paraffin. (Fig. 227.) In such cases only the chlorine preparations are promising.



FIG. 226.—Comparison of oils. Observe the degree of effect. Each area received 0.01 c. c. of 3 per cent solution of dichlorethylsulphide in the oil, spread over a surface of about one-half inch diameter. The photograph was taken 2 days after application. The solvent oils were as follows: 110, liquid petrolatum; 111, raw linseed oil; 112, boiled linseed oil; 113, olive oil; 114, castor oil; 115, cod-liver oil. (The figures refer to experiments.)

PROTECTIVE VARNISHES *

These may be supposed to act like the fats. They would remain longer on the skin, but they can only be applied in a very thin coat, and this is likely to furnish only an incomplete protection. A thicker coating might soon become harmful.

The actual tests by the vapor method, although not complete, were not encouraging.

Aluminum paint (83) actually increased the irritation; asphalt-ether varnish (80) was no better than bare skin. Collodion (85) furnished a very slight protection.

The following protected, but it was not determined whether the protection was greater than that of simple oiling: Rosin-ether varnish; also with zinc stearate and with fuller's earth; shellac varnish.

* The numbers in parentheses refer to experiments

ADSORBENT POWDERS

These were found highly effective, just as they are in the masks. A layer of 1 mm. thick protects completely against the vapor test (Fig. 228) and quite effectively against the alcoholic solution. The results were as follows:

Vapor tests on dry powders (Sollmann).—Bare skin erythematous papule. No lesion followed on cocoanut charcoal (29). Slight and inconstant erythema (less than linseed oil 53): Kaolin (27, 73), fuller's earth (28, 74). Slight papular erythema: Zinc stearate (30) (about like liquid petrolatum 47).

Vapor tests on dry powders (Loucks).—Bare skin erythematous papule. No lesions followed on: Manganese dioxide (103), talcum (108), zinc oxide (105). Slight erythema: Silver abietate (107); reduced iron (104), litharge (106). Moderate erythema: Zinc stearate (107).

Liquid test with alcoholic dichlorethylsulphide.—Fuller's earth protected most; talcum, intermediate protection; calcium carbonate, least protection.

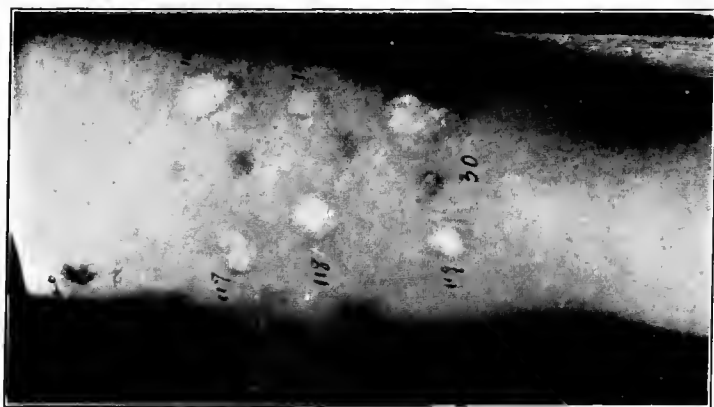


FIG. 227.—Protective value of dichloramine-T. Pieces of filter paper about 5 mm. square, and containing about 0.001 c. c. of 95 per cent dichlorethylsulphide were applied to the center of a square of skin, covered with the protectives. The coatings were as follows: 117, raw linseed oil; 118, linseed oil and kaolin, 1 to 3; 119, same with 3 per cent of soft soap; 120, petrolatum kaolin, 1 to 1; 121, dichloramine-T, 10 per cent in ehloresane; 122, solid paraffin. The photographs were made 1 day after the application. Note that the reaction is less in 121 than in the others; 26 and 30 are rerudescences of lesions 25 days old. (The figures refer to experiments.)

These results show that the general efficiency of the powders is as follows, the most effective being at the beginning, the least effective at the end of the list: Cocoanut charcoal; fuller's earth, kaolin; talcum, manganese dioxide, zinc oxid; silver abietate, reduced iron, litharge; zinc stearate; calcium carbonate.

Practically the usefulness of the adsorbent powders is limited by the difficulty of keeping them on the skin in sufficient thickness.

The above tabulation of relative efficiency indicates plainly that the following act only mechanically, and not chemically, and that this efficiency is actually lower than that of the cheaper charcoal, kaolin, or fuller's earth, namely, metallic soaps (zinc stearate), metallic resinate (silver abietate), metallic oxids (zinc oxid and litharge), and free metals (reduced iron).

ADSORBENT WATER PASTE

The attempt was made to secure a better adhesion of the adsorbents to the skin by using them in the form of pastes. These pastes are not nearly as efficient as the dry powders. This is explainable partly by the deleterious effects of water itself, and partly by the watery film, preventing ready access of the nearly insoluble dichlorethylsulphide to the adsorbent.

The following experiments were made, the results again being presented in order, the most efficient above, the least effective below.

Vapor tests (Sollmann).—Bare skin gives erythematous papule.

Inconstant slight erythema: Cocoa-charcoal paste (67) (about like dry kaolin).

Papular erythema, rather less than on bare skin: Powdered zinc paste (71).

About as on bare skin: Fuller's earth paste (68).

Slightly more severe than on bare skin: Kaolin paste (66).

Complete vesication: Sodium bicarbonate paste (64).

Water alone produces more severe blister and scabbing (63).

Vapor tests (Cassel).—Collargol, 10 per cent (93) did not furnish protection, giving the same results as on the bare skin.

Liquid alcoholic dichlorethylsulphide.—Alkresta (purified fuller's earth) in 50 per cent glycerin (16) furnishes a fair protection, while 50 per cent glycerin alone increases vesication (15).

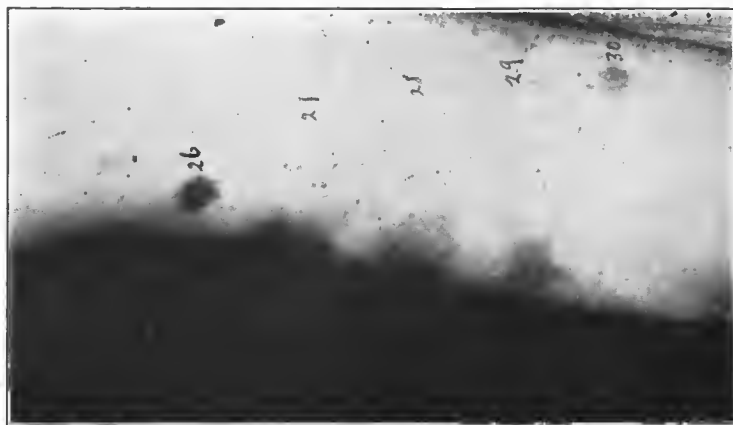


FIG. 228.—Efficiency of dry powders. Dichlorethylsulphide vapor was applied. Note the normal lesion in the bare skin (26); the slight protection afforded by zinc stearate (30); and the complete protection from kaolin, fuller's earth, and charcoal (indicated by the absence of lesions in a straight line drawn from 26 to 30). The photograph was taken 3 days after the application. (The numbers in parenthesis refer to experiments.)

SOAPS

Plain soap.—"Soft soap" furnishes considerable protection, chiefly, it is presumed, by acting as a solvent. It acted as well as linseed oil or zinc oleate in the vapor test (65). It may also be incorporated with the ointments; for instance, 5 per cent with petrolatum (91), and 3 per cent in the linseed kaolin mixture (119). The addition of the soap modifies ointments so that they can be applied more smoothly and also facilitates their removal by washing. These advantages, however, are not very great, and it is conceivable that the alkalinity of the soaps might injure some skins.

Metallic soaps.—Certain reports by other workers indicated that metallic soaps and resins would be especially effective. This was not confirmed. Those tried had only a limited success, and this was attributable mainly to their mechanical action as absorbents and fillers.

PLASTER

Lead plaster (54).—Protected well in the vapor test, but this was explained by the dense consistence of the film.

OINTMENTS

Zinc oleate (the old U. S. P. preparation).—Protected partially in the vapor test, being about equal to linseed oil (53) and very little better than kaolin-petrolatum ointment (50). On another subject (97) it protected completely, but so did ointment of zinc oxide or boric acid.

Zinc stearate in the dry form (30, 107).—Protects very little, even against vapor; much less than dry kaolin (28), talcum (108), or zinc oxide.

Zinc stearate petrolatum ointment.—Furnished protection against vapor (95), but so did similar ointments of zinc oxide (96) and boric acid (99).

Silver abietate (resinate), dry.—This furnished only a relatively slight protection against vapor (107), being inferior to talcum (108).

Silver abietate-petrolatum ointment.—This protects against the vapor (101), but so did a similar boric acid ointment (99).

POWDERED AND COLLOIDAL METALS AND METALLIC OXIDES

These were tried in the hope that they might act as catalysts, accelerating the hydrolysis of the dichlorethylsulphide. The results show that this does not occur under the conditions of their use on the skin. They furnish some protection, but no more than any indifferent powders. The following were tried:

In dry powder form.—Powdered zinc (79): Protection against vapor much less than dry kaolin (73). Manganese dioxide (103) and zinc oxide (105): Protect against vapor, but so did talcum (108).

As water pastes.—Zinc dust paste (71): Protects very little better than fuller's earth paste (68), both being about the same as on the bare skin (62). Collargol, 10 per cent (93): Does not protect.

As petrolatum ointments.—Zinc dust ointment: Protects somewhat better than petrolatum; but probably not better than any indifferent powder, such as hexamethylanamin (20). Manganese dioxide ointment (98), zinc oxide ointment (96), and collargol ointment (94): Protect against vapor, but so did boric ointment (99).

CHLORINE PREPARATIONS

The caustic action of dichlorethylsulphide is destroyed by further chlorination. Chlorinated lime and the chloramines are effective under working conditions. Their efficiency is limited; and their practical application is further confined by their irritant action on the skin, the instability of some of the preparations, and the cost of the chloramines.

Their efficiency is illustrated by Figure 227 and by the following experiments:

In the vapor tests.—Complete protection was secured by: Dichloramine-T, dry (76), or in water paste (69), or as 10 per cent dusting powder (78) and 10 per cent in chlorcosane. Calx chlorinata, in the same forms (75, 70, 77). The efficiency of dichloramine-T and calx chlorinata was equal to that of dry charcoal, and superior to all others. Chloramine-T paste, Squibb (52), gave almost complete protection.

Against concentrated liquid G34.—Dichloramine-T, 10 per cent in chlorcosane gave only partial protection (121), but was somewhat more efficient than linseed kaolin pastes (118, 119). This is shown in the Figure 227.

CHAPTER XVIII

OINTMENT PROTECTION AGAINST MUSTARD GAS^a

Dichlorethylsulphide was so extensively used on the Western Front and caused so large a number of casualties in consequence of its skin irritating properties that great effort was made to protect against skin burns due to this gas. The majority of burns were apparently due to vapor, although many, constituting a small percentage, were due to the liquid. Statistics on the relative number of liquid and vapor burns in the field are not available.

In the protection of the skin against dichlorethylsulphide burns two propositions were involved: (1) The protection of the skin against burning by droplets of the liquid, and (2) protection against vapors of dichlorethylsulphide.

Again, in protection against dichlorethylsulphide, there was to be considered the protection of men in factories in which the gas was being produced and in the filling stations, and the protection of soldiers in the field against dichlorethylsulphide used by the enemy. It soon developed in the course of the investigations that it was impossible to protect the skin by means of any ointment or skin dressing against burning by droplets of the liquid. Moreover, it also developed early that the only protection which should be offered to men in factories and filling stations was in the nature of protective clothing and gloves. A large amount of work was done on this subject at the American University, University of Wisconsin, and elsewhere, but this discussion is confined to the consideration of protection by ointments.

The first efforts were directed toward the development of an impervious paint, which soon proved to be entirely impracticable since it was uncomfortable, cracked, and interfered with the normal functioning of the skin. A number of investigators then sought to find an ointment which, when placed on the skin, would offer partial or complete protection against burns by vapor of dichlorethylsulphide.

Among the protective varnishes studied were the following: Shellac, aluminum paint, asphalt ether, and collodion. These substances either offered no protection at all or actually increased the irritation produced by the dichlorethylsulphide.

The following protective films were then studied: Raw linseed oil, boiled linseed oil, olive oil, castor oil, cocoanut oil, linoleic acid, oleic acid, paraffin, cod-liver oil, petrolatum, soy-bean oil, peanut oil, lanolin, liquid petrolatum, turpentine.

Since none of these protective films were sufficiently serviceable, it was sought to increase their protective power by incorporating other material. In most instances, no chemical reaction was possible between dichlorethylsulphide and the substances incorporated, and these are named first: Cocoanut charcoal, fuller's earth, talcum, magnesium oxide, zinc oxide, zinc stearate, zinc oleate, calcium carbonate, silver abietate, calcium hydroxide, manganese resinate, soap and calcium sulphide, soap and agar agar, soap and gum tragacanth, green soap, egg albumin, gelatin, flaxa liquid soap, reduced iron, soap, tannic acid, powdered zinc, collargol, glycerin (50 per cent), glucose, soap and albumin, soap and gum acacia, soap and glycerin, carnauba wax, litharge.

^a These investigations were conducted by the section of pharmacology and toxicology, Research Division, Chemical Warfare Service

The following substances, which would presumably react with dichlorethylsulphide and destroy it, were used: Hexamethylene tetramine, bleaching powder (calcium hypochlorite), chloramine-T, dichloramine-T, tincture of iodine, potassium permanganate.

METHOD OF TESTING THE VALUE OF PROTECTIVE OINTMENT

The method which was used in studying the value of protective ointments improved as the work progressed. Wilson and Fuller, who did the largest volume of work on the subject, described the following method of testing in their later work:¹ An area of 1 by 3 inches was marked off on the skin of the forearm. This area was treated with 0.1 c. c. of the ointment. Except for a short time immediately after the application of the ointment, no effort was made to prevent rubbing of the treated area by the clothing. A test tube $4\frac{1}{2}$ by $\frac{1}{2}$ inch was inclosed in a second larger test tube to obtain an air space around the inner tube. A tightly packed piece of glass wool was introduced into the inner tube about 2 inches from the open end. About 1 c. c. of pure dichlorethylsulphide was dropped onto this wool. In making this exposure, the stopper was removed from the inner tube so that the area to be tested was only in contact with the open end of the inner test tube. Exposures were made for a definite length of time, using a stop watch. The period of time elapsing between the application of the ointment and exposure to the vapor varied in these experiments. The area exposed to the dichlorethylsulphide was circular and measured one-half inch in diameter. Other much more accurate methods of studying the effect of vapors of skin irritants were devised in connection with other work,² but they were not used in connection with protective ointment.

The individual was given a similar burn on an unprotected portion of the skin, and an attempt was made to estimate the degree of protection offered by the ointment by comparing the burn produced through the ointment with that produced on the bare skin. The ointment on the bare skin was given a value of 100, and then the degree of burning through the ointment was estimated on this basis. A 100 per cent burn would mean that the ointment offered no protection; a 50 per cent burn would mean that the burn was only one-half as severe. Using this method, Wilson and Fuller developed ointment No. 146 as the best protection. This substance has the following composition:

	Parts by weight
Zinc oxide (100 mesh, U. S. P.)-----	45
Benzoated lard-----	10
Refined raw linseed oil-----	30
Hydrous lanolin (adeps lanæ, U. S. P.)-----	15
Coloring matter to give flesh color.	

The method of manufacture was briefly as follows: The zinc oxide was thoroughly mixed with the linseed oil, and benzoated lard containing sufficient coloring matter was then added to the mixture of zinc oxide and linseed oil. Finally the lanolin was added and the whole thoroughly mixed.

It was directed that the soldier should apply the ointment twice a day when exposure to vapor of dichlorethylsulphide was anticipated, but not to the entire body. He was directed merely to apply it to the crotch, the armpits, hands and feet, and exposed portions of the face.

The theory of the protective action of ointments of the class represented by ointment No. 146 is as follows: The dichlorethylsulphide, being soluble in fats, would pass into the ointment and remain there as long as the exposure to dichlorethylsulphide continued. On removal from the vapor the dichlorethylsulphide would supposedly evaporate again into the air and protection would thus be afforded. It was found that all those substances which reacted with dichlorethylsulphide and destroyed it were too irritating to apply to the skin. The method of testing used in the work was not satisfactory because of the small area of skin exposed to the gas. It is obvious that a small area of skin deleteriously affected by exposure to an irritant but surrounded by healthy skin would show less effect than a similar area of skin surrounded by tissue similarly affected. Thus, a small area might not show a blister on exposure to a given concentration, whereas a larger area might readily blister. The only satisfactory method of determining the protective value of an ointment is by sending an individual into a chamber containing a definite and known concentration of the vapor and exposing a sufficiently large surface of his skin to the action of gas. By a sufficiently large area is meant one-half or one-fourth of a forearm. The rest of the body could be protected by means of special protective clothing and a mask. When this test was applied to ointment No. 146, it was found to be extremely doubtful whether it offered any protection at all against such concentrations of dichlorethylsulphide as would probably be encountered in the field, and it was the conviction of those who examined these burns that the ointment was of little or no value. It may be stated, therefore, that no satisfactory ointment for protection against burns by vapors of dichlorethylsulphide was found.

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- (2) Eyster, J. A. E., and Maver, Mary E.: An Apparatus for the Exposure of Skin or Mucous Membrane to the Vapor of Toxic Substances, with Observations on Dichlorethylsulphide. *Journal of Pharmacology and Experimental Therapeutics*, Baltimore, Md., 1920-21, xv, No. 2, 95.

CHAPTER XIX

THE EXPERIMENTAL TREATMENT OF POISONING BY LUNG IRRITANT OR SUFFOCANT GASES ^a

CHLORINE

In chlorine poisoning gassed dogs fall naturally into two chief classes: Dogs which die within three days (acute deaths) as a result of changes directly induced by the gas; and dogs which survive this acute period (survivals) and recover or later succumb to secondary factors, chiefly pneumonia. It is obvious that in the treatment of chlorine poisoning attention should be focused on the prevention or alleviation of the acute effects—the direct results of the action of the chlorine—and the success of the treatment should be judged by the total number of survivors, that is, those living through the acute period, rather than by actual recoveries, since infection and the other factors which prevent the recovery of most of the survivors are merely incidental to the gassing.

In the investigation of the physiological action of chlorine it was imperative frequently to draw samples of blood after gassing. Though the quantity of blood drawn at any one time was small, it was noted that many of the animals seemed to be favorably influenced by the experimental procedure.

Venesection, of course, has long been employed in conditions involving pulmonary edema and congestion. Recently it has been applied, with conflicting results, in the treatment of these conditions induced in man by poisonous gases in warfare. Inasmuch as the incidental observations with blood letting indicated a favorable influence upon gassed dogs it was deemed desirable to determine, under exact conditions, the effect of venesection upon the mortality of dogs receiving a lethal concentration of chlorine gas.

EFFECT OF VENESECTION ALONE

A series of twenty dogs, which had been gassed at a lethal concentration ^b by the standard method, were studied to determine the effect of venesection on chlorine poisoning. Blood to the amount of not less than 1 per cent of the body weight was drawn from each animal soon after exposure. It was assumed, on account of the rapid development of serious symptoms, that it was imperative to treat the animals as soon as practicable after gassing. Obviously it is easier to inhibit the establishment of an abnormal state than to alleviate the condition when fully established. However, variations up to two hours in the time of treatment apparently play little rôle in its efficacy.

The blood was drawn, without anesthesia, by aspiration through a needle inserted through the skin into a jugular vein. This procedure was carried out easily and without discomfort to the animal. In most cases the blood was

^a The data in this chapter are based on investigations made by the Medical Division, Chemical Warfare Service, at Yale University, New Haven, Conn., and published by Lieut. Col. Frank P. Underhill, C. W. S., in: *The Lethal War Gases, Physiology and Experimental Treatment*, Yale University Press, 1920.

^b From 800 to 900 parts chlorine per million of air (2.53 to 2.85 mgm. per liter) for a period of one-half hour.

drawn all at one time, but in a few instances it was removed by several small bleedings. In either case the general result was the same, as was determined by separate analysis of the data and accordingly all the data are included together in Table 64. The standard toxicity figures are given for comparison. It is apparent from the table that 35 per cent of the animals which had been bled survived the acute period as compared with 13 per cent survivals for the untreated animals. The percentage of dogs that died acutely was decreased from 87 per cent to 65 per cent. These figures indicate clearly the therapeutic value of venesection after chlorine poisoning in dogs under the conditions of the experiment.

TABLE 64.—*Effect of venesection on chlorine poisoning after standard gassing*

	Untreated	Bled 1 per cent or more of body weight
Deaths:		
First day.....per cent.....	52	40
Second day.....do.....	26	15
Third day.....do.....	9	10
Total acute deaths.....do.....	87	65
Delayed deaths.....do.....	4	5
Recoveries.....do.....	9	30
Survivals.....do.....	13	35
Number of dogs.....	23	20

The result is at variance with that reported by British investigators upon goats. But it should be emphasized in the present experiment upon dogs that the bleeding was performed early (usually from one-half to two hours after gassing) and therefore before the onset of severe symptoms. At times it was observed that experimental animals died acutely during treatment. In all cases the animal struggled violently and in several instances death occurred before any attempt was made at manipulative procedure, bleeding or otherwise. Under these conditions it would seem that the observed collapse was caused by failure of the heart, a resultant of violent struggling rather than venesection. Furthermore, it should be observed in this connection that the conclusions reached are based on the actual death or survival of the animals experimented on and that the gassing procedure was carried out under carefully controlled conditions which permitted accurate comparison with previously determined toxicity figures.

EFFECT OF VENESECTION PLUS INFUSION

Having established the therapeutic value of venesection, attempts were made to determine measures to still further increase the percentage of survivals. Infusion of physiologic salt solution is distinctly indicated when large volumes of blood are withdrawn. Under these circumstances the salt solution tends toward the temporary maintenance of the normal blood volume and helps to maintain in equilibrium other important functions. Furthermore, the thickened condition of the blood subsequent to gassing suggested the infusion for its probable diluent effect. Therefore, a series of 15 gassed dogs were bled 1 per cent of body weight and immediately thereafter were infused with warm isotonic

sodium chloride solution, equal in volume to the blood withdrawn. The infusion was accomplished by inserting a needle under aseptic conditions through the skin into the jugular vein. The solution was allowed to flow slowly from a burette.

The results (Table 65) show 40 per cent of survivals as compared with 35 per cent survivals for venesection alone, and 13 per cent for the untreated series. Conversely the acute deaths are reduced to 60 per cent as compared with 65 per cent for venesection alone and 87 per cent for the untreated dogs.

TABLE 65.—*Effect of venesection and infusion of salt solution*

Treatment	Untreated (standard toxicity)	Bled	Bled and infused isotonic NaCl
Deaths:			
First day.....per cent.....	52	40	60
Second day.....do.....	26	15	0
Third day.....do.....	9	10	0
Total acute deaths.....do.....	87	65	60
Delayed deaths.....do.....	4	5	20
Recoveries.....do.....	9	30	20
Survivals.....do.....	13	35	40
Number of dogs used.....	23	20	15

A closer analysis of the data, however, for each of the three days which comprise the acute period is suggestive. It will be noted that, while both bleeding alone and bleeding plus infusion markedly reduced the total acute deaths (deaths during first three days) as compared with those in the untreated series, and, while bleeding plus infusion showed a greater reduction in this regard—and therefore was more efficacious, judged by the standard of this investigation—than bleeding alone, nevertheless bleeding plus infusion showed a much greater number of deaths during the first 24 hours and no deaths during the remainder of the acute period. In other words, the infused sodium chloride apparently had a deleterious effect on the most severely poisoned dogs—i. e., the dogs which, if untreated, would have succumbed acutely—in that it brought about the death of all within the first 24 hours after exposure, while it had a decidedly beneficial effect on another group of animals, presumably less severely affected by the gas, and successfully tided them over the three-day period and put them into the group of survivals.

Therefore the results from this experiment establish beyond peradventure that venesection is a valuable therapeutic measure, and indicate that venesection plus infusion of sodium chloride is better. Furthermore, the analysis of data for the respective 24-hour periods suggests that measures must be sought to save at least the percentage of untreated animals which are forced, as it were, from the latter part of the acute period into the first 24 hours.

Accordingly, the effect of substituting the infusion of isotonic acid, alkaline and neutral solutions of other salts in place of sodium chloride was investigated. The chief results are given in Table 66, from which it is apparent that both Na_2HPO_4 and Na_3PO_4 gave at least as high a percentage of survivals as sodium chloride. But Na_3PO_4 , as well as NaH_2PO_4 , gave rise to marked respiratory disturbances and so were not considered further. Na_2HPO_4 , however, offered a suggestive lead, since this alkaline solution gave a slightly higher percentage of survivals than sodium chloride.

TABLE 66.—*Influence of various salt solutions in the treatment of chlorine poisoning*

[Recorded by percentages]

	Untreated	Bled	Bled and infused isotonic				
			(I) NaCl	(II) Na ₂ HPO ₄	(III) NaH ₂ PO ₄	(IV) Na ₃ PO ₄	(V) Neutral mixture
Deaths:							
First day.....per cent..	52	40	60	43	67	40	74
Second day.....do.....	26	15	0	14	0	20	10
Third day.....do.....	9	10	0	0	0	0	10
Total acute deaths.....do.....	87	65	60	57	67	60	94
Delayed deaths.....do.....	4	5	20	14	0	20	0
Recoveries.....do.....	9	30	20	29	33	20	6
Survivals.....do.....	13	35	40	43	33	40	6
Number of dogs used.....	23	20	15	14	6	10	19

(I) 0.95 to 1.0 per cent NaCl.

(III) 1 c. c. = 5.00 mgm. P.

(V) pH 7.4. Solutions not isotonic.

(II) 4.5 per cent Na₂HPO₄, 0.12 H₂O.(IV) 1 c. c. = 4.00 mgm. P Δ = -57.

EFFECT OF VENESECTION, INFUSION, AND ADMINISTRATION OF SODIUM BICARBONATE

Investigation of the urine after chlorine poisoning shows that there is a characteristic increase of acidity and an augmented excretion of ammonia, acid phosphates, and organic acids. All of these indicate acidosis. In addition, this is substantiated by direct determination of the bicarbonate value of the blood. Since alkali administration is suggested in all conditions where an acidosis is present, a study was made of the influence of sodium bicarbonate (5 to 10 gm. in 50 to 200 c. c. of water) per os, in conjunction with venesection and infusion of sodium chloride.

The results on a series of 28 dogs are summarized in Table 67. The animals given the sodium bicarbonate after bleeding and infusion show a distinctly greater percentage of survivals, 54 per cent as compared with 40 per cent for those merely bled and infused. Also, the latter series shows 60 per cent acute deaths, while the bicarbonate treated series shows only 46 per cent acute deaths. It is to be noted again, however, that there was still the tendency, though by no means so marked, for acute deaths to be forced, as it were, from the later to the early part of the three-day acute period—there being more acute deaths during the first day after gassing followed by bleeding plus infusion and bicarbonate than after bleeding alone—though the net result of the former method is decidedly more beneficial.

TABLE 67.—*Treatment of chlorine poisoning*

	Untreated	Bled	Bled and infused isotonic NaCl	Bled and infused isotonic NaCl NaHCO ₃ per os
Deaths:				
First day.....per cent..	52	40	60	43
Second day.....do.....	26	15	0	3
Third day.....do.....	9	10	0	0
Total acute deaths.....do.....	87	65	60	46
Delayed deaths.....do.....	4	5	20	25
Recoveries.....do.....	9	30	20	29
Survivals.....do.....	13	35	40	54
Number of dogs.....	23	20	15	28

From the investigation of therapeutic measures as thus far outlined, it is clear that bleeding is beneficial; that bleeding plus infusion of isotonic sodium chloride solution is more beneficial; and that bleeding and infusion plus the administration of sodium bicarbonate per os is most beneficial, since, under the conditions of the experiment, 54 per cent of animals survived after the latter treatment as compared with 13 per cent of survivals for the untreated series.

EFFECT OF VARIOUS MODIFICATIONS OF THE TREATMENT

Attempts were then made to improve the treatment further by variations in the concentration of the infused sodium chloride solution; variations in the volume of the infused chloride solution; the infusion of isotonic nonelectrolytes; the substitution of other infusion fluids for the sodium chloride; other methods.

VARIATIONS IN THE CONCENTRATION OF THE SODIUM CHLORIDE INFUSION FLUID

Forty dogs were given the treatment outlined above except that the concentration of the sodium chloride solution was slightly hypotonic or hypertonic. The results (Table 68) show at a glance that the infusion of the slightly hypotonic and hypertonic solution of sodium chloride is markedly inferior to isotonic solutions, the survivals varying from 16 per cent to 35 per cent for the former as compared with 54 per cent for the latter. In fact, non-isotonic infusion is less beneficial than venesection without infusion at all. Emphasis, therefore, should be placed upon the necessarily narrow limits of concentration allowable in the infusion fluid.

TABLE 68.—*The influence of various strengths of sodium chloride solutions in the treatment of chlorine poisoning*

[Recorded by percentages]

	Untreated	Bled	Bled plus NaHCO ₃ per os; infused NaCl solution			
			Isotonic	Hypotonic	Hypertonic	
			0.95-1.0 per cent	0.7 per cent	1.3 per cent	1.75 per cent
Deaths:						
First day.....per cent	52	40	43	57	50	67
Second day.....do	26	15	3	7	14	17
Third day.....do	9	10	0	7	0	0
Total acute deaths.....do	87	65	46	71	64	84
Delayed deaths.....do	4	5	25	29	21	8
Recoveries.....do	9	30	29	0	14	8
Survivals.....do	13	35	54	29	35	16
Number of dogs.....	23	20	28	14	14	12

VARIATIONS IN THE VOLUME OF THE INFUSED SODIUM CHLORIDE SOLUTION

Twenty-eight dogs were studied in order to determine whether the infusion of smaller or larger volumes of sodium chloride solution than the volume of the blood (1 per cent of body weight) withdrawn would improve the treatment. In this series sodium bicarbonate was not administered. Comparing the figures obtained with those for one volume of sodium chloride infusion without bicarbonate administration shows unquestionably that infusion of more or less

solution than blood withdrawn is far less beneficial (Table 69). Experiment also demonstrated (Table 70) that repeating the saline infusion 7 to 10 hours after the first treatment does not increase the percentage of survivals above the figure obtained by single treatment.^c

TABLE 69.—*The influence of the volume of fluid injected in the treatment of chlorine poisoning*

	Bled and infused isotonic NaCl solution		
	1 volume	$\frac{1}{2}$ volume	2 volumes
Deaths:			
First day.....per cent..	60	45	65
Second day.....do.....	0	27	6
Third day.....do.....	0	9	6
Total acute deaths.....do.....	60	82	76
Delayed deaths.....do.....	26	9	6
Recoveries.....do.....	20	9	18
Survivals.....do.....	40	18	24
Number of dogs.....	15	11	17

TABLE 70.—*The influence of repeated infusion in the treatment of chlorine poisoning*

	Bled, NaHCO ₃ per os infused isotonic NaCl solution	
	One infusion	Infusion repeated
	<i>Per cent.</i>	<i>Per cent.</i>
Deaths:		
First day.....per cent..	43	37
Second day.....do.....	3	16
Third day.....do.....	0	5
Total acute deaths.....do.....	46	58
Delayed deaths.....do.....	25	21
Recoveries.....do.....	29	21
Survivals.....do.....	54	42
Number of dogs used.....	28	19

INFUSION OF ISOTONIC NONELECTROLYTES

The infusion of solutions of nonelectrolytes such as isotonic dextrose alone and 3 to 6 per cent gum acacia in isotonic saline (1 to 3 infusions) was also found to increase the acute mortality as well as decrease the survivals as compared with the standard toxicity figures for untreated animals (Table 71).

TABLE 71.—*The influence of dextrose and acacia solutions in the treatment of chlorine poisoning*

[Recorded by percentage]

	Untreated	Bled, NaHCO ₃ per os infused			
		NaCl isotonic	Dextrose, 5.5 per cent	Acacia 6 per cent isotonic NaCl	Acacia 3 per cent isotonic NaCl
Deaths:					
First day.....per cent..	52	43	73	43	67
Second day.....do.....	26	3	27	58	0
Third day.....do.....	9	0	0	0	11
Total acute deaths.....do.....	87	46	100	100	78
Delayed deaths.....do.....	4	25	0	0	0
Recoveries.....do.....	9	29	0	0	22
Survivals.....do.....	13	54	0	0	22
Number of dogs used.....	23	28	11	7	9

^c Note that in this experiment NaHCO₃ was administered.

SUBSTITUTION OF OTHER INFUSION FLUIDS FOR ISOTONIC SODIUM CHLORIDE

A series of 13 dogs was infused with Ringer's solution with double the usual amount of calcium. Another series of 15 dogs was infused with isotonic Na_2SO_4 . Both of these fluids were markedly less beneficial than isotonic sodium chloride (cf. Table 72).

TABLE 72.—*The influence of calcium and other salts in the treatment of chlorine poisoning*
[Recorded by percentage]

	Untreated	Bled plus NaHCO_3 per os infused		
		Isotonic NaCl	Ringer's solution, double calcium content	Isotonic 2 per cent Na_2SO_4
Deaths:				
First day.....per cent.....	52	43	77	60
Second day.....do.....	26	3	0	7
Third day.....do.....	9	0	15	7
Total acute deaths.....do.....	87	46	92	74
Delayed deaths.....do.....	4	25	8	7
Recoveries.....do.....	9	29	0	20
Survivals.....do.....	13	54	8	27
Number of dogs.....	23	28	13	15

OTHER PROCEDURES TESTED

Morphine (5 mgm. per kilo) was administered to 10 dogs in addition to the prescribed treatment and found to be distinctly harmful. In this series the survivals were only 10 per cent as compared with 54 per cent for dogs receiving the regular treatment alone and 13 per cent for untreated animals (Table 73). Another series of 18 animals was treated in an entirely different manner. To 8 dogs 5 to 10 grams of NaHCO_3 was administered by stomach, sound bleeding and infusion being omitted. This treatment was without beneficial effect (Table 74), the total acute deaths and the survivals being the same as for untreated animals. The 10 other dogs of the series were merely bled 1 per cent and then given a subcutaneous infusion of 1 per cent calcium chloride in 0.5 per cent sodium chloride solution, according to the method outlined in the "Translation of Captured German Document." This procedure was found to increase the percentage of total acute deaths and decrease the percentage of survivals as compared with that for animals which received no treatment whatsoever (Table 74).

TABLE 73.—*Effect of morphine in treatment of chlorine poisoning*

	Untreated	Bled, NaHCO_3 per os infused	
		Isotonic NaCl	Isotonic NaCl plus morphine (0.5 mgm per kilo)
Deaths:			
First day.....per cent.....	52	43	60
Second day.....do.....	26	3	30
Third day.....do.....	9	0	0
Total acute deaths.....do.....	87	46	90
Delayed deaths.....do.....	4	25	0
Recoveries.....do.....	9	29	10
Survivals.....do.....	13	54	10
Number of dogs used.....	23	28	10

TABLE 74.—*The influence of subcutaneous injections of calcium in the treatment of chlorine poisoning*

[Recorded by percentage]

	Untreated	Bled, infused isotonic NaCl NaHCO ₃ per os	NaHCO ₃ per os	Bled, 1 per cent CaCl ₂ in 0.5 per cent NaCl solution subcutaneously
Deaths:				
First day.....per cent.....	52	43	63	60
Second day.....do.....	26	3	12	30
Third day.....do.....	9	0	12	0
Total acute deaths.....do.....	87	46	87	90
Delayed deaths.....do.....	4	25	0	10
Recoveries.....do.....	9	29	12	0
Survivals.....do.....	13	54	12	10
Number of dogs.....do.....	23	28	8	10

EFFECT OF ENVIRONMENTAL CONDITIONS (TEMPERATURE) ON THE EFFICACY OF THE PRESCRIBED TREATMENT

Finally, a study was made of the effect of environmental conditions, chiefly temperature, on the efficacy of the prescribed treatment. Throughout the definitive experiments, every endeavor was made to keep the gassed animals under as favorable conditions as possible. However, one series of 10 dogs was allowed to become chilled after exposure to the gas, and another series of 9 dogs was kept at a relatively low temperature. Both series received the prescribed treatment. The data (Table 75) show 20 per cent survivals for the "chilled" and zero survivals for the "cold" series as compared with 54 per cent survivals for the regular series kept under favorable temperature conditions. The result is a conclusive demonstration of the important part played by external temperature in determining the survivals and recoveries after gassing.

TABLE 75.—*Effect of environmental conditions (temperature) on the efficacy of the prescribed treatment*

[Recorded by percentage]

	Bled and infused isotonic NaCl NaHCO ₃ per os		
	Kept warm	Chilled	Cold
Deaths:			
First day.....per cent.....	43	70	100
Second day.....do.....	3	10	0
Third day.....do.....	0	0	0
Total acute deaths.....do.....	46	80	100
Delayed deaths.....do.....	25	20	0
Recoveries.....do.....	29	0	0
Survivals.....do.....	54	20	0
Number of dogs.....do.....	28	10	9

SUMMARY OF STUDIES OF TREATMENT

The investigation just described of therapeutic measures for chlorine poisoning involved the study of over 300 dogs gassed at the standard lethal concentration ^d as worked out in the laboratory. It is obvious that the acute symptoms of chlorine poisoning are most prominent in dogs gassed at this concentration.

^d From 800 to 900 parts chlorine per million of air (2.53 to 2.85 mgm. per liter) for a period of one-half hour.

Therefore, it must be emphasized that the intensive changes induced by this lethal concentration put to the most rigorous test any method of treatment of the condition. A treatment which is reasonably successful at this lethal concentration may be expected to produce much greater results when administered in conditions less severe; that is, in animals exposed to lower concentrations of chlorine gas.

Again, environmental conditions, such as temperature, are crucial factors in determining the efficacy of therapeutic measures.

THERAPEUTIC PROCEDURES TRIED

Over 20 different therapeutic procedures were tried. These may be classified, on the basis of the data already presented, as follows:

DISTINCTLY BENEFICIAL

(a) Bleeding, infusion of isotonic sodium chloride solution in volume equal to the blood withdrawn, administration of NaHCO_3 by stomach sound (Table 68). (b) Bleeding, infusion of isotonic Na_2HPO_4 solution (Table 66). (c) Bleeding alone (Table 64).

LESS BENEFICIAL OR WITHOUT BENEFICIAL EFFECT

(a) Bleeding, infusion of hypertonic or hypotonic sodium chloride solution, NaHCO_3 by mouth (Table 68). (b) Bleeding, infusion of isotonic sodium chloride solution repeated 7 to 10 hours after the original treatment, NaHCO_3 by mouth (Table 70). (c) Bleeding, infusion of isotonic sodium chloride solution in one-half or double the volume of the blood withdrawn (Table 69). (d) Bleeding, infusion of isotonic NaH_2PO_4 or Na_3PO_4 solution (Table 66).^c (e) Bleeding, infusion of isotonic Na_2SO_4 solution, NaHCO_3 by mouth (Table 72). (f) Administration of NaHCO_3 by stomach sound (Table 74).

DISTINCTLY HARMFUL

(a) Bleeding, infusion of isotonic sodium chloride solution, NaHCO_3 by mouth, morphine (0.5 mgm. per kilo) (Table 73). (b) Bleeding, infusion of isotonic dextrose solution, NaHCO_3 by mouth (Table 71). (c) Bleeding, infusion of 3 or 6 per cent gum acacia in isotonic saline solution, NaHCO_3 by mouth (Table 71). (d) Bleeding, infusion of neutral PO_4 mixture (Table 66). (e) Bleeding, subcutaneous infusion of 1 per cent calcium chloride in 0.5 per cent sodium chloride (Table 74). (f) Bleeding, infusion of Ringer's solution with double quantity of calcium, NaHCO_3 by mouth (Table 72).

Therefore, the investigation leads unmistakably to the conclusion that, under the conditions of the experiments, the first therapeutic method of those listed as "distinctly beneficial" is the one in which emphasis should be placed. This prescribed method may be restated as follows:

(1) Venesection, involving the withdrawal of approximately 1 per cent of the body weight. (2) Intravenous infusion of warm sterile isotonic solution equal in volume to the blood withdrawn. (3) Administration of NaHCO_3 by a stomach tube—5 to 10 grams in 50 to 100 cubic centimeters of water. Treatment to be carried out from one-half to two hours after exposure to the gas.

^c The figures indicate a large increase in survivals, as compared with the untreated animals, but marked respiratory disturbances rendered the use of these salts inadvisable.

PHOSGENE

It was not until a study of phosgene poisoning was made that an adequate conception was obtained of the fundamental principles involved in gas poisoning. The treatment for chlorine poisoning was evolved by more or less empirical methods, whereas in the case of phosgene the changes taking place in the blood were well recognized and the stages of phosgene poisoning quite clearly defined previous to any extensive attempts at therapeutic measures. This understanding of the problem led to a much more rational plan of attack with regard to treatment.

It is of interest that the treatment for phosgene formulated on this plan was in principle the same as outlined for chlorine poisoning except that the time factor varied. With chlorine poisoning early bleeding and early infusion of salt solution were advocated. With phosgene early bleeding and late infusion were imperative. With chlorine a significant acidosis was present; hence, alkali by mouth was indicated. Inasmuch as acidosis failed to be manifested in phosgene poisoning except as a terminal acidosis, the administration of sodium bicarbonate was omitted.

Since the time of infusion is directly indicated by the abnormally high concentration of the blood, a rapid method of determining blood concentration is essential. Blood concentration and hemoglobin content follow similar courses. Determination of hemoglobin, therefore, gives an exact indication of blood concentration and hence a means of determining when salt infusion should be made in order to restore concentrated blood to more normal conditions. A further indication of the condition of the animal is found in the temperature changes, which should be followed at one-half hour periods.

TREATMENT IN FIRST STAGE

Approximately one hour after gassing, blood is drawn from a vein to the extent of 1 per cent of the body weight. Bleeding at any time up to four hours after gassing is beneficial, but the best results are obtained when the withdrawal of blood is practiced about one hour after gassing.

TREATMENT IN SECOND STAGE

In the first stage, blood concentration may exhibit one of two features after bleeding: (a) The blood becomes markedly dilute and slowly returns to normal concentration; (b) there is no significant dilution of the blood. The latter is an exceptional condition. The time of treatment, therefore, will depend upon which of these two conditions obtains. When the blood becomes markedly dilute and then slowly returns to the normal, infusion of 0.97 per cent sodium chloride solution equal in amount to the blood withdrawn should be practiced when the concentration reaches the normal level. This usually takes from 8 to 10 hours. On the other hand, when even after bleeding the concentration of the blood is not definitely decreased, infusion of salt solution should be delayed until there is a clear indication that the blood is becoming concentrated. This usually occurs from 6 to 8 hours after gassing. In any case the infusion should not be delayed beyond the point where the blood has reached a concentration of more than 25 per cent above normal.

In following blood concentration, estimations of hemoglobin are made at intervals of an hour.

After the infusion of salt solution the concentration of the blood is followed at one-hour intervals in order to determine whether subsequent salt infusions are

indicated. In general after the first infusion the blood may begin to concentrate again within one hour, and when this concentration continues it may be desirable to infuse subsequently, but judgment must be exercised in order to strike a proper mean between insufficient and excessive infusion. Insufficient infusion leaves the blood concentrated. Excessive infusion augments edema. So long as the concentration of the blood remains constant, infusion is unnecessary, and when the concentration diminishes the animal is on the road to recovery.

TREATMENT IN THIRD STAGE

Usually rest and warmth are all that are necessary in this stage; but if the blood should become greatly diluted again and remain so, a second bleeding may be necessary. This condition, however, rarely occurs.

OBSERVATIONS LEADING TO METHOD OF TREATMENT

The adoption of early bleeding as a therapeutic measure in phosgene poisoning was made with the idea that it would be beneficial in preventing excessive dilution of the blood and would relieve the heart of the strain placed upon it by a significantly increased blood volume. This view was adopted previous to actual determinations of blood volume. It will be remembered that Eyster and Meek (Chap. XI) claim blood volume is not increased. If this is true then early bleeding plays little rôle with regard to the original conception. However, it is quite possible to interpret the beneficial effects of bleeding on the assumption that thereby pulmonary edema is modified in that extraction of considerable quantities of blood makes it more difficult for the organism to obtain from its tissues fluid sufficient to furnish an intensive edema. In other words, one must assume that bleeding tends to delay or inhibit blood concentration. It will be shown that this actually occurs.

From toxicity experiments it may be accepted that phosgene in concentrations of 70 to 80 parts per million (0.30 to 0.35 mgm. per liter) may be regarded as the lethal concentration.

THE TIME ELEMENT IN BLEEDING

The experience had been gained in phosgene poisoning that acute symptoms do not appear so rapidly as they occur with chlorine. It became, therefore, a matter of particular importance to determine whether early bleeding or later bleeding was more beneficial in the treatment of phosgene poisoning. To test this point bleeding was practiced at a period of one hour in one series of animals and at a period of five hours in a second series, one series comprising 38 animals, the other 30. The results are shown in Table 76.

TABLE 76.—*The influence of the element of time of bleeding in the treatment of phosgene poisoning*
[Phosgene concentration, 71 to 80 (0.31 to 0.35 mgm. per liter)]

	Toxicity	Bled 1 per cent in—	
		1 hour	5 hours
Deaths:			
First day.....per cent.....	36	26	33
Second day.....do.....	19	16	10
Third day.....do.....	9	0	0
Total acute deaths.....do.....	64	42	43
Delayed deaths.....do.....	8	8	10
Recoveries.....do.....	28	50	47
Survivals.....do.....	36	58	57
Number of dogs used.....	53	38	30

It is quite evident from these figures that bleeding is decidedly beneficial in phosgene poisoning and that there is very little difference either in acute deaths or ultimate recoveries of the animals bled one hour or five hours after gassing. One may conclude that it is immaterial whether bleeding is practiced at one or five hours after gassing.

THE INFLUENCE OF MULTIPLE SMALL BLEEDINGS

It is possible that repeated small bleedings (20 to 30 c. c. at frequent intervals) would exert equal or greater beneficial effects upon dogs gassed with phosgene than a single venesection. In Table 77 the results of such an investigation are recorded for different concentrations of phosgene.

TABLE 77.—*The influence of multiple small bleedings*

[Recorded by percentage]

	Concentrations					
	61-70 (0.26-0.30 mgm.)		71-80 (0.31-0.35 mgm.)		81-90 (0.35-0.39 mgm.)	
	Toxicity	Bled	Toxicity	Bled	Toxicity	Bled
Deaths:						
First day.....per cent.....	17	9	36	35	54	45
Second day.....do.....	25	0	19	15	18	27
Third day.....do.....	0	9	9	12	2	9
Total acute deaths.....do.....	42	18	64	62	70	82
Delayed deaths.....do.....	12	9	8	0	9	0
Recoveries.....do.....	46	63	28	38	21	18
Survivals.....do.....	58	72	36	38	30	18
Number of dogs used.....	24	11	38	26	56	11

It is quite apparent that multiple small bleedings tended to have a beneficial influence at a concentration 61 to 70 (0.26 to 0.30 mgm. per liter) phosgene. The total acute deaths were reduced from 42 per cent to 18 per cent, and the recoveries increased from 46 per cent to 63 per cent. Beyond this concentration, however, the favorable effect of this procedure was apparently lost.

THE EFFECT OF EARLY INFUSION WITH AND WITHOUT PREVIOUS VENESECTION

Although convinced that early infusion was not directly indicated, tests of its influence were made first by infusion of isotonic salt solution alone one hour after gassing, and in a second series of animals venesection one hour after gassing, followed immediately by infusion of salt solution. In both experiments salt solution to approximately 1 per cent of the body weight was introduced. (Table 78.) These data demonstrate that infusion of 0.97 per cent sodium chloride solution to the extent of 1 per cent of the body weight one hour after gassing is distinctly detrimental in phosgene poisoning. It is also quite evident that the results were not as good as those obtained with bleeding only after one hour. The conclusion may be drawn, therefore, that immediate infusion is detrimental under the experimental conditions.

TABLE 78.—*Influence of early infusion (recorded by percentage)*

[Concentration, phosgene 71 to 80 (0.31 to 0.35 mgm. per liter)]

	Toxicity	Infused 1 per cent 0.97 per cent NaCl in 1 hour	Bled only	Bled 1 hour and infused 1 per cent 0.97 per cent NaCl
Deaths:				
First day.....per cent.....	36	53	26	40
Second day.....do.....	19	18	16	7
Third day.....do.....	9	0	0	3
Total acute deaths.....do.....	64	71	42	50
Delayed deaths.....do.....	8	0	8	7
Recoveries.....do.....	28	29	50	43
Survivals.....do.....	36	29	58	50
Number of dogs used.....do.....	53	17	38	30

EARLY BLEEDING AND DELAYED INFUSION

When venesection was practiced one hour after exposure to phosgene and infusion of salt solution was made at a period when blood concentration was occurring rapidly, results were obtained as recorded in Table 79. Of these 35 dogs only 30 received infusion, inasmuch as 5 animals died previous to the time when it was possible to introduce the salt solution. It is quite evident, therefore, that the figures do not adequately express the influence of the procedure. If only those animals receiving infusion are included, then the total recoveries are significantly increased and the animals living beyond the three-day period are increased from 58 per cent with bleeding alone to 80 per cent with bleeding plus delayed infusion. Even without consideration of these 5 dogs, delayed infusion after early bleeding noticeably reduces death even though ultimate recoveries are not increased over bleeding alone.

TABLE 79.—*Influence of early bleeding and delayed infusion*

[Concentration, phosgene 70 to 80 (0.30 to 0.35 mgm. per liter)]

	Toxicity	Bleeding only	Bleeding and de- layed infusion
Deaths:			
First day.....per cent.....	36	26	14
Second day.....do.....	19	16	14
Third day.....do.....	9	0	3
Total acute deaths.....do.....	64	42	31
Delayed deaths.....do.....	8	8	20
Recoveries.....do.....	28	50	49
Survivals.....do.....	36	58	69
Number of dogs used.....do.....	53	38	35

EXPERIENCE WITH HIGHER CONCENTRATIONS

In order to put the method of treatment to an even greater test observations were made on dogs gassed at a concentration of 80 to 90 parts phosgene (0.35 to 0.39 mgm. per liter) per million of air. The results are presented in Table 80. In these experiments the animal was bled 1 per cent of its body weight one hour after gassing, and then if it seemed desirable, bleeding to the extent of one-half of 1 per cent was later practiced. Water was given freely. It will be seen that at this concentration a single large bleeding did not yield results much better than the toxicity figures. Bleeding followed by immediate infusion was distinctly detrimental, as were multiple infusions. Bleeding plus delayed infusion, when emphasis is placed upon a definite time after gassing for infusion rather than an exact adherence to the degree of concentration of the blood, gave the results seen in column 5, Table 80. These are little better than bleeding alone. This observation is a clear indication that in order to yield the best results definite criteria of the animal's condition must be followed closely and the kind and time of treatment should be practiced in strict accord with these criteria. When changes in temperature and hemoglobin were employed in this connection, and treatment was given to dogs gassed with phosgene at a concentration of 80 to 90 (0.35 to 0.39 mgm. per liter) parts per million of air, results such as those presented in column 6 were obtained. Obviously these observations lead to the conclusion that the method of treatment herein outlined is rendered decidedly efficacious when careful consideration is given to the time element with respect to infusion. In these results in certain instances more than one infusion was given at times, the number being determined entirely by the response of the change in hemoglobin. If after a single infusion the blood concentration again rapidly increased, a second or even a third infusion was given. Column 7 in Table 80 shows that even when the blood concentration and temperature are not followed so closely, excellent results may be obtained by following the method in general. One reason for the poorer results shown in column 7 of Table 80 is that in a number of animals included the wrong strength of salt solution was employed, every animal receiving it dying.

TABLE 80.—*Influence of various types of treatment (recorded by percentage)*

[Concentration, phosgene 80 to 90 (0.35 to 0.39 mgm. per liter)]

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
	Toxicity	Single bleeding	Infused immediately	Multiple infusion	Delayed infusion	Exact treatment	Less exact treatment	Infused 1.02 per cent NaCl according to hemoglobin
Deaths:								
First day.....per cent..	54	43	70	54	38	30	44	91
Second day.....do.....	14	13	10	31	20		2	
Third day.....do.....	2	7	10		3		2	
Total acute deaths.....do.....	70	63	90	85	61	30	48	91
Delayed deaths.....do.....	9	7		15	6	7	4	9
Recoveries.....do.....	21	30	10		33	63	48	
Survivals.....do.....	30	37	10	15	39	70	52	9
Number of dogs used.....	56	30	20	13	36	30	48	11

In this connection attention should be called to the necessity of infusion of the correct strength of sodium chloride solution. Excellent results were yielded when this salt solution varied in strength from 0.95 per cent to 0.98 per cent. Variations on either side of these limits were attended with detrimental effects. Thus in Table 80, column 8, it may be seen that when dogs were infused with sodium chloride solution of a strength of 1.02 per cent all died, even though, in every other respect, the treatment given was in strict accord with the prescribed method.

MODIFIED METHOD OF TREATMENT

The final step in the method of treatment was the recognition that it was unnecessary to infuse every animal exposed to phosgene and, further, that by early repeated bleeding the number of gassed animals needing infusion could be appreciably reduced. Moreover, the possibility was presented that, inasmuch as the essential feature of infusion is to dilute the blood even though only temporarily, the same result could be obtained by introducing water by routes other than by direct infusion, namely, by the mouth or intraperitoneally.

The following considerations are pertinent with respect to the modified procedure:

The change in hemoglobin of the blood and the temperature curve may be accepted as accurate criteria of the condition of the gassed dog.

These criteria may be depended upon as indicators of the time for treatment and the type of treatment.

Intensive treatment in the first state (that is, during the period of blood dilution) of phosgene poisoning, in the majority of cases, will prevent extreme concentration of the blood characteristic of the second stage. In other words, the second stage is very greatly modified by proper treatment of the first stage. During the first stage water should not be given.

Proper treatment of the first stage consists in venesection to the extent of 0.5 per cent body weight as soon as practicable after gassing. The temperature and hemoglobin are then followed at one-half hour intervals. So long as the temperature remains normal and blood concentration does not diminish further treatment is not indicated. When, however, the temperature rises rapidly and a fall in blood concentration occurs (the two changes take place simultaneously) a second venesection of 0.5 per cent body weight is practiced. This procedure may be repeated for the second time, that is, until blood to the extent of 1.5 per cent of the body weight has been withdrawn.

The large majority of cases needed no further treatment and practically every animal survived.

If in spite of intensive treatment in the first stage, the blood became markedly concentrated and a marked fall in temperature took place, the condition of the animal was considered as very serious, and if left untreated it would surely die.

Under these conditions two types of treatment were carried through: (a) To those animals that would drink, large quantities of water were given, or water was given by a sound; (b) infusion or intraperitoneal injection of 0.95 per cent sodium chloride solution was practiced.

Probably 50 per cent of animals in a serious condition in the second stage might be saved by following either procedure.

Injudicious infusion of salt solution might be markedly detrimental, hastening the onset of death. Judicious infusion of salt solution resulted in the survival of a large number of animals.

Infusion of salt solution was necessary only with the most serious cases, and a considerable degree of judgment had to be employed.

Finally, the aim of treatment in phosgene poisoning should be to consider each case as an entity, and to give treatment only in accordance with changes in temperature and hemoglobin, the criteria of changes in the gassed animal's condition.

In Table S1 will be found the observations made with the modified treatment. It may be concluded that the results yielded are almost as good as the best obtained when every animal was infused, and that the modified method is more practical under field conditions than would be a method where intravenous injection is necessary. From a practical viewpoint then, this modification is of considerable importance. Equally important practically is the fact that not every animal needs even water introduction, the blood concentration being controlled in large measure by the early repeated bleeding. It is significant that by following the modified method delayed deaths are entirely eliminated.

TABLE S1.—*Modified treatment*
[Concentration, phosgene 81 to 90 (0.35 to 0.39 mgm. per liter)]

	Toxicity	Water by mouth	Intra-peritoneal infusion
Deaths:			
First day.....per cent.....	54	47	37
Second day.....do.....	14	0	12
Third day.....do.....	2	0	0
Total acute deaths.....do.....	70	47	49
Delayed deaths.....do.....	9	0	0
Recoveries.....do.....	21	53	51
Survivals.....do.....	30	53	51
Number of dogs used.....do.....	56	15	33

INFLUENCE OF WATER INTAKE OF ANIMAL UPON PHOSGENE TREATMENT

It was deemed desirable to determine what influence upon phosgene treatment would be exerted by changing the water intake of an animal previous to gassing. The results may be seen in Table S2. If water was withheld from a dog 48 hours previous to exposure to phosgene, response to treatment is very poor. In other words, water starvation previous to gassing exerted a distinctly detrimental effect. The administration of water just previous to exposure to gas gave results entirely comparable with those of the toxicity figures. In other words, too much water was also definitely detrimental. When water administration constituted the only treatment, little or no improvement over the toxicity figures was observed.

TABLE S2.—*Influence of water intake upon treatment*
[Concentration, phosgene 81 to 90 (0.35 to 0.39 mgm. per liter)]

	Toxicity	48 hours water starvation	Water just previous to gassing	Water administration only treatment
Deaths:				
First day.....per cent.....	54	40	38	44
Second day.....do.....	14	40	19	22
Third day.....do.....	2	7	6	0
Total acute deaths.....do.....	70	87	63	66
Delayed deaths.....do.....	9	0	6	6
Recoveries.....do.....	21	13	31	28
Survivals.....do.....	30	13	37	34
Number of dogs.....do.....	56	15	15	18

DOES INFUSION OF SALT SOLUTION AGGRAVATE EDEMA?

In certain quarters objection was raised to the injection of salt solution on the ground that such infusion would tend to aggravate edema and hence perhaps exert a detrimental influence. From the experiments carried through by Capt. Samuel Goldschmidt and Capt. David Wright Wilson, of the Chemical Warfare Service, at Porton, England, with goats (see Chapter XX), it may be stated that this objection is without foundation. Goats gassed with phosgene, bled and infused with sodium chloride solution, gave no evidence that this procedure aggravated the existing edema. These results were obtained by determination of the lung to heart (L:H) ratio with and without infusion, and if edema were actually increased by the infusion the change would surely be indicated by alterations in this ratio. The results follow:

	Untreated	Treated
Number of goats dying after time of treatment.....	17	18
Average length of life of animals that died (days).....	2.2	2.3
Average L: H ratios of animals that died.....	8.6	7.7
Number of animals surviving the acute period.....	13	13
Average L: H ratios of animals surviving the acute period.....	4.4	3.8

The average L:H ratios were slightly less in the animals that had been treated, both in the groups that died and in those which survived. Goats dying after being treated by venesection alone failed to show any marked difference in the L:H ratios. Therefore, the conclusion may be drawn that infusion does not increase the edema of the lungs in phosgene poisoning. Indeed, the evidence indicates that the edema is somewhat decreased.

CHLOROPICRIN

The treatment of chloropicrin poisoning was carried through upon both dogs and goats. In the latter instance the observations were made at Porton,^f England, by Captain Goldschmidt and Captain Wilson.

EXPERIMENTS WITH GOATS

The method of gassing may be outlined briefly. Ten or 12 goats were placed in the gassing chamber and left for a period of 25 minutes in an atmosphere of chloropicrin, made by spraying in the liquid in quantities sufficient to develop a theoretical concentration of from 1 part of chloropicrin in 8,500 to 9,000 parts of air. The air in the chamber was kept continually in motion during the period of the gassing by means of an electric fan.

The animals were arbitrarily divided into two equal groups; one group was treated, while the other served as a control. An effort was made to have, so far as possible, an equal division of animals as regards weight and sex, in the two groups. This division was made without any reference to the animal, before the gassing was completed, and adhered to regardless of the condition of the respective animals after gassing.

Bleeding was performed by aspiration through a needle inserted through the skin into the right or left jugular vein. This procedure was performed so far as practicable under aseptic precautions.

^f We are greatly indebted to Lieut. Col. Crossley and Mr. Joseph Barcroft for placing these facilities at our disposal as well as for many helpful suggestions and criticisms.

One bleeding only was made one hour after the animals were removed from the chamber.

All of the animals which survived were kept under careful observation for a period of 5 to 7 days, and then sacrificed for post-mortem examination. As nearly 90 per cent of the mortalities occurred within the first 24 hours, and most of the surviving animals improved rapidly thereafter, the length of the period of observation is considered ample. Hence it may be safely stated that life or death has been the criterion of the beneficial effect of the treatment employed.

A large number of experiments were performed, but for present purposes only those groups in which from 60 to 100 per cent of the goats in the control group died are selected. Tables S3 and S4 give the results of these experiments.

TABLE S3.—*Effect of bleeding in goats gassed with chloropicrin*

[1:8,500 to 1:9,000 for 25 minutes]

	Animals used	Deaths	Percentage deaths
Untreated.....	48	43	90
Treated.....	47	27	57

TABLE S4.—*Effect of bleeding upon goats gassed with chloropicrin*

[1:8500 to 1:9000 for 25 minutes]

	3 to 8 hours	8 to 24 hours	24 to 28 hours	2 to 7 days	Total deaths	Survivals
Animals grouped according to time of death:						
Untreated.....	19	18	2	4	43	5
Treated.....	8	16	1	2	27	20
Animals surviving at beginning of period:						
Untreated.....	48	29	11	9		
Treated.....	47	39	23	22		
Percentage deaths among animals surviving at beginning of period:						
Untreated.....	40	62	18	44		
Treated.....	17	41	4	9		

As may be seen in Table S3, the mortality of the treated animals is decreased from 90 per cent to 57 per cent by a single bleeding in a severely gassed goat. This large reduction in mortality in the 95 animals used in these experiments demonstrates conclusively that bleeding is an efficacious therapeutic procedure when applied early to goats gassed with high concentrations of chloropicrin. These data have been subjected to statistical analysis and found to be conclusive.

Table S4 shows the percentage deaths (expressed as per cent of animals surviving at the beginning of each period) of experimental and control animals at four periods after gassing. The first critical period occurred within 8 hours after gassing. An inspection of Table S4 shows that whereas 40 per cent of the control animals had died at this time but 17 per cent of the treated animals had succumbed at this period.

The next and more critical period lay between 8 and 24 hours. Here also a greater percentage of the untreated animals died. Hence a single treatment had furnished protection for the treated animals through the severest portion of the acute stage of the gassing. After 24 hours the number of treated animals

which died was very small; on the other hand, the untreated continued to give an appreciable percentage of deaths. It may, therefore, be concluded that the treatment gave a permanent advantage, and did not merely delay the death of the animal.

Unfortunately the observations upon goats were not sufficiently extended to show the influence of infusion upon this animal.

EXPERIMENTING WITH DOGS

The first type of treatment which was tried with dogs subjected to chloropicrin poisoning was multiple bleeding. In Series I (Table 85) of this treatment 21 dogs were treated which had been gassed at a concentration of 0.81 to 0.95 mgm. per liter, and in Series V 41 dogs which had been gassed at a concentration of 0.96 to 1.10 mgm. per liter. The animals, as soon as received from the gassing chamber, generally about a half hour after the close of gassing, were bled one-half per cent of body weight. The animals were followed every hour for hemoglobin. If the hemoglobin showed a concentration the animal was bled another one-half per cent of body weight, and further concentration was followed by further bleeding.

TABLE 85.—*Chloropicrin treatment*
(Concentration of chloropicrin, 111 to 131 (0.81 to 0.95 milligram per liter)

	Toxicity	Series I (21 dogs)		Series II (11 dogs)		Series III (9 dogs)		Series IV (15 dogs)	
		Number of dogs	Per cent	Number of dogs	Per cent	Number of dogs	Per cent	Number of dogs	Per cent
Deaths:	<i>Per cent</i>								
First day.....	30	9	43	6	54	2	22	0	0
Second day.....	17	1	5	0	0	2	22	2	13
Third day.....	6	0	0	0	0	0	0	1	7
Total deaths in 3 days.....	53	10	48	6	54	4	44	3	20
Delayed deaths.....	4	1	5	0	0	0	0	0	0
Recoveries.....	43	10	47	5	46	5	56	12	80
Survivals.....	47	11	52	5	46	5	56	12	80

(Concentration of chloropicrin, 132 to 151 (0.96 to 1.10 milligrams per liter)

	Toxicity	Series V (41 dogs)		Series VI (9 dogs)		Series VII (9 dogs)	
		Number of dogs	Per cent	Number of dogs	Per cent	Number of dogs	Per cent
Deaths:	<i>Per cent</i>						
First day.....	55	27	66	4	45	2	22
Second day.....	8	0	0	1	11	1	11
Third day.....	2	1	2	0	0	0	0
Total deaths in 3 days.....	65	28	68	5	56	3	33
Delayed deaths.....	2	0	0	0	0	0	0
Recoveries.....	33	13	32	4	44	6	67
Survivals.....	35	13	32	4	44	6	67

As shown in Table 85, the results obtained from this type of treatment at both concentrations were practically identical with the regular toxicity figures, and it appears clear, considering the large number of animals used, that this type of treatment is of no benefit.

The fundamental idea of this treatment is that if the animals are bled as the blood concentrates, additional fluid will be supplied from the tissues, and as a result the blood will become less concentrated. So far as one can tell this does not happen. The records, in general, give no evidence that the multiple bleedings bring down the concentration of the blood, and in fact in some cases at least it continues to increase more rapidly than without bleeding. It appears probable that as soon as the edema begins to develop in the lungs, with a consequent loss of fluid from the blood, that the tissues are immediately called upon to supply additional fluid. As long as fluid is supplied from the tissues in this manner, the concentration of the blood will be kept to a minimal figure, but as soon as the fluid reserve of the tissues is exhausted the concentration of the blood will increase in exact ratio to the development of edema in the lungs. Inasmuch then as the fluid reserve of the tissues has been used by this time it appears logical to suppose that additional bleeding would only further aggravate the concentration and this is apparently what happens.

DESCRIPTION OF TREATMENT USED

SERIES I.—Multiple bleeding. Animals bled one-half per cent of body weight within one-half hour after close of gassing. Further bleeding of same amount upon concentration of blood.

SERIES II.—No bleeding. Animals given 2 per cent of body weight of H_2O by stomach tube within one-half hour after close of gassing. Further fluid supplied according to hemoglobin and clinical symptoms.

SERIES III.—Bled 1 per cent of body weight within one-half hour after gassing and given 2 per cent H_2O by stomach tube immediately after bleeding. Additional fluid supplied by intravenous or intraperitoneal infusion of isotonic saline solution indicated by hemoglobin or clinical symptoms.

SERIES IV.—Same as Series III except animals were bled one-half per cent of body weight instead of 1 per cent.

SERIES V.—Same as Series I.

SERIES VI.—Bled 1 per cent and given intravenous infusion of 1 per cent isotonic saline within two hours after close of gassing.

SERIES VII.—Same as Series IV.

In Series II the animals were not bled, but were given 2 per cent of body weight of water by stomach tube within an hour after gassing. The treatment of this series was just the opposite of that in Series I. To counteract the concentration of the blood, fluid was supplied at once which could be absorbed into the blood stream, and the blood thus kept at a lower concentration. The recoveries by this treatment were only very slightly above the toxicity figures.

In Series IV and VII, the final treatment adopted, the animals were bled one-half per cent of body weight within a half hour after the close of gassing and 2 per cent water was given to the animal at once by stomach tube. The animals were closely followed, and in case a need of further fluid was indicated by hemoglobin or temperature it was supplied. Fifteen animals which had been gassed at a concentration of from 0.81 to 0.95 mgm. per liter and (Series VII) nine animals which had been gassed at a concentration between 0.96 to 1.10 mgm. per liter were treated by this method. Out of the 15 animals at the lower concentration, there were no deaths the first day and only three deaths

altogether, giving a percentage of recoveries of 80 per cent. At the higher concentration there were two deaths the first day and one the second day, leaving 6 animals which recovered, or practically 67 per cent. The percentage survivals in this treatment series was very much greater than in the regular toxicity groups.

This same treatment was tried, with the exception that the animals were bled 1 per cent of body weight instead of one-half per cent. As shown in Series III nine animals were thus treated, of which five recovered, giving a percentage recovery of about 56 per cent, as compared with 80 per cent when the one-half per cent bleeding was used. Although the number of animals used in this series was small the results clearly indicated that the one-half per cent bleeding was the better.

In Series VI nine dogs which had been gassed at a concentration of 0.96 to 1.10 mgm. per liter were bled 1 per cent of body weight and given an intravenous infusion of 1 per cent of body weight of normal saline immediately afterwards, the whole process taking place within two hours after gassing and at the time when the blood began to concentrate. The percentage of survivals for this was 44 per cent, which is an increase of 12 per cent over regular toxicity recoveries, and a decrease of 23 per cent when compared with the final adopted treatment as given in Series VII.

The final treatment, as given above, in Series IV and VII, appears to be a logical one when the condition of a gassed animal is considered. The bleeding of one-half per cent of body weight is not sufficient to weaken the animal in any way, but *a priori* would appear to be efficacious in two ways. In the first place, providing any toxic substances had been taken up by the blood, as a result of gassing, the bleeding serves to relieve the blood of a certain amount of these substances. In the second place, the bleeding initiates influx of new fluid from the tissues into the blood. As the edema in the lungs develops and the blood concentrates, the influx continues until the fluid reserve of the tissues, augmented by the 2 per cent of body weight of water given at the time of bleeding has been depleted, or, in the less serious cases, until the edema of the lungs has ceased to develop.

In the animals which were seriously affected this basic treatment of bleeding and supplying of fluid by mouth or intraperitoneally was not sufficient to save the animals. Evidently in such cases the edema of the lungs continues to develop so rapidly that even the augmented fluid reserve becomes exhausted. In serious cases of this type it was found that an intravenous injection of about 1 per cent of body weight of normal saline would, at once in many cases, reduce the concentration of the blood to such an extent that the animal would be carried through the period of rapid edema development. Such an infusion can be repeated if necessary.

It is quite obvious that from the data the most efficacious method of treatment in chloropicrin poisoning is to bleed one-half per cent of the body weight as soon as possible after gassing and then at once administer water by way of the mouth. Additional fluid may be supplied later by intravenous infusion of sodium chloride solution in accord with hemoglobin readings and temperature changes. With this treatment there are no "delayed deaths."

OXYGEN IN THE TREATMENT OF POISONING BY LUNG-IRRITATING GASES

Clinical experience in gas poisoning leads to the conclusion that lack of oxygen plays a significant rôle in this condition. This inference has been confirmed by experimental evidence and various possibilities may be cited as causes for the establishment of anoxemia. Thus it is possible that the inflammatory changes in the lungs may hinder the absorption of oxygen. Vascular obstruction in the lungs, owing to swelling of the alveolar tissues, and the development of edema may also result in poor oxygen absorption; or again, there may be an irregular distribution of air in the lungs, owing to shallow breathing or partial obstruction of some of the bronchi. Any one or all of these conditions may operate to decrease oxygen absorption. All of these possibilities, however, carry with them the assumption that there is an inadequate oxygenation of the blood, meaning thereby an insufficient supply of oxygen in the arterial blood. According to experimental results there is little or no evidence of an inadequate supply of oxygen in the arterial blood during the first part, if not the whole, of the first period of phosgene poisoning. When, however, blood concentration becomes marked insufficient oxygen in the arterial blood is quite apparent. In a previous section of this chapter emphasis has been laid upon changes in blood concentration as the responsible factor leading to the condition of anoxemia. According to this view the viscosity of the concentrated blood leads to impaired circulation through the tissue capillaries thus accounting for the abnormally low oxygen content of the venous blood. Oxygen lack in the arterial blood is not present to the same degree.

From these observations it becomes apparent that the need for oxygen in the first period of phosgene poisoning is not great. In the second period, however, oxygen lack becomes quite pronounced, especially in the venous blood. The question naturally arises: Will administration of oxygen eliminate anoxemia? Again, if anoxemia is alleviated will this allow an individual to survive the effects of phosgene poisoning? In other words, is inadequate oxygenation of the blood responsible for death? From clinical experience there seems to be conflicting evidence as to the value of oxygen in the treatment of phosgene poisoning. On the whole, however, it would appear that the consensus of opinion indicates that oxygen administration is decidedly beneficial in the circumstances under discussion.

THE INFLUENCE OF OXYGEN ADMINISTRATION UPON PHOSGENE POISONING

In order to ascertain whether oxygen administration is of therapeutic value dogs gassed with the lethal concentration of phosgene (70 to 80 parts per million of air; 0.30 to 0.35 mgm. per liter) were placed in a respiratory chamber through which oxygen was circulated. The concentration of oxygen selected was 50 per cent, small variations from this figure occurring during the course of the experiments. Analysis of the air in the chamber was made from time to time. The dogs were placed in the chamber 2 to 5 hours after gassing and kept there continuously up to a period of 72 hours. This period was selected for the reason that it was chosen as the limit of the duration of the acute stage of poisoning. Arrangements were made for the absorption of carbon dioxide and regulation of moisture and temperature within the chamber. Water was supplied to the experimental animal.

The investigation was carried out upon 30 dogs to which oxygen was administered. A control series of 27 animals gassed at the same concentration but without any treatment, except that they were kept quiet and warm in the same room with the experimental dogs, was also observed. (Table 86.)

TABLE 86.—*The influence of oxygen administration upon the mortality of dogs gassed with phosgene*

	Oxygen series		Control series (no oxygen)	
	Number of dogs	Per cent	Number of dogs	Per cent
Deaths in—				
24 hours.....	17	57	17	63
2 days.....	2	6	3	11
3 days.....	0	0	0	0
Total acute deaths.....	19	63	20	74
Delayed deaths.....	2	20	1	14
Recoveries.....	9	27	6	22
Survivals.....	11	47	7	36
Number of dogs.....	30		27	

The results indicate, under the experimental condition, that: (1) In both series by far the larger percentage of deaths occurred within the first 24 hours. (2) All the animals that died (exclusive of "delayed deaths") did so within 48 hours. (3) Oxygen increased but slightly the percentage of survivals, from 26 per cent to 37 per cent. (4) Oxygen had even less effect on prolonging the life of the dogs beyond the first 24 hours. (5) Oxygen did not increase the number of dogs that survived the "acute period" to die later of secondary causes. (6) Oxygen did not markedly increase the percentage of dogs that ultimately recovered.

If, instead of employing the exact controls, comparison is made between the so-called "toxicity figures" and the results obtained with oxygen administration, the beneficial influence of oxygen upon dogs gassed with lethal concentrations of phosgene is entirely lacking. The results, especially with respect to the survivals beyond the acute period and the ultimate recoveries, were almost identical (Table 87).

TABLE 87.—*Comparison of toxicity figures for phosgene and those obtained by oxygen administration*

[Concentration of phosgene, 71 to 80 (0.31 to 0.35 mgm. per liter)]

	Toxicity figures	Oxygen figures
Deaths in—		
24 hours.....per cent.....	36	57
2 days.....do.....	19	6
3 days.....do.....	9	0
Total acute deaths.....do.....	64	63
Delayed deaths.....do.....	8	10
Recoveries.....do.....	28	27
Survivals.....do.....	36	37
Number of dogs.....	53	30

Although these figures are very striking, too much emphasis should not be laid upon them, inasmuch as the number of animals employed in the two series were too dissimilar. This comparison, however, emphasizes the fact, revealed by the comparison with the actual control series, that continuous oxygen administration after phosgene poisoning did not appreciably decrease the percentage of deaths nor can it be said to have materially prolonged life. There is the same difference present that may be obtained when two series of animals are gassed by different observers under unlike environmental conditions. Though this conclusion is inevitable from the data it must be conceded that oxygen administration seemed to relieve the animal. It rested more quietly, respiration was less difficult and obvious cyanosis disappeared or was absent. From the failure of oxygen to prolong life in spite of obvious improvement in clinical symptoms it would appear that such a therapeutic measure does not alleviate the fundamental difficulty in phosgene poisoning.

THE INFLUENCE OF OXYGEN ADMINISTRATION UPON THE MORTALITY OF GASED DOGS TREATED BY VENESECTION

Thirty dogs were gassed with a lethal concentration of phosgene (71 to 80 parts per million, or 0.31 to 0.35 mgm. per liter of air) and one hour later 1 per cent of the body weight of blood was withdrawn from the jugular vein or from the femoral artery, in both cases without anesthesia. The animals were then placed in the oxygen chamber and kept there up to 72 hours. The results of these observations may be seen in Table 88, where a comparison is made with the effects of bleeding alone. It is quite obvious from these results that bleeding plus oxygen administration as a therapeutic measure has no appreciable advantage over simple venesection. Although carried through by different men in separate laboratories at different times of the year, the results in the two series of observations have a striking similarity, both of kind and degree.

TABLE 88.—*The influence of oxygen upon gassed dogs treated by venesection*

	With oxygen		Without oxygen (per cent)
	Number of dogs	Per cent	
Deaths in—			
24 hours.....	6	20	26
2 days.....	4	13	16
3 days.....	4	13	0
Total acute deaths.....	14	46	42
Delayed deaths.....	1	6	8
Recoveries.....	15	50	50
Survivals.....	16	56	58
Number of dogs.....	30		38

THE INFLUENCE OF OXYGEN ADMINISTRATION UPON THE MORTALITY OF DOGS GASED WITH A SUBLETHAL CONCENTRATION OF PHOSGENE

Of a series of 14 dogs gassed at a concentration of 50 to 60 parts of phosgene per million parts of air (0.21 to 0.26 mgm. per liter) for one-half hour and treated with oxygen, 57 per cent survived beyond the three-day period. The toxicity figure is 54 per cent. Oxygen can be said, therefore, to have no bene-

ficial effect on dogs gassed at a concentration lower than "lethal." This is corroborated when the recoveries in the two cases are compared—43 per cent with treatment as against 44 per cent without treatment (Table S9).

TABLE S9.—*Influence of oxygen upon dogs gassed with sublethal concentrations of phosgene and treated by venesection*

	With oxygen	Without oxygen
Deaths in—		
24 hours..... per cent..	14	26
2 days.....do.....	0	13
3 days.....do.....	29	8
Total acute deaths.....do.....	43	47
Delayed deaths.....do.....	14	10
Recoveries.....do.....	43	44
Survivals.....do.....	57	54
Number of dogs.....do.....	14	39

The next logical step would have been to discover the influence of oxygen administration upon the final prescribed treatment for phosgene poisoning, namely, venesection followed by infusion of sodium chloride solution.

Just before it was imperative to discontinue the work a series of experiments was started in this direction from which results of a positive nature were anticipated. In this series the dogs were bled 1 per cent of their body weight, as soon after gassing as possible, followed at a proper time by an infusion of warm, sterile, isotonic (0.95 per cent) NaCl, and the dogs then placed in the oxygen apparatus. When the outcome of the work dealing with the study of the blood-oxygen after gassing, the dog breathing air as compared with breathing oxygen, before and after bleeding, and before and after infusion is read (see p. 711), it will be realized why the carrying out of this series seemed to be so promising of results. The particular point involved was the ability of the gassed dog to get hold, as it were, of the additional amount of oxygen provided, as well as of that in atmospheric air, as evidenced by the arterial and venous oxygen content when infusion was carried out. Three dogs only were thus treated. The first died just under 72 hours after gassing, the other two recovered.

OBSERVATIONS ON THE ADMINISTRATION OF OXYGEN TO DOGS GASED WITH CHLORINE

The administration of oxygen to chlorine dogs placed in the circulating apparatus was substantially the same as used for phosgene, except that since the work on chlorine was done first the apparatus was not as complete as it was later.

Three dogs were given oxygen, with no previous treatment, after gassing. Of these none survived. The first died on the second day; the other two on the first day.

Eight dogs were given oxygen after treatment as developed at the time. Within one-half hour after gassing, the dogs were bled 1 per cent of their body weight by aspiration from the jugular vein. The same amount of warm, sterile, isotonic (0.95 per cent) sodium chloride was then slowly infused, after which 50 cubic centimeters of 10 per cent NaHCO_3 were given by a stomach tube.

The dog was then placed in the oxygen box, and the concentration of oxygen in the circulating air gradually raised to approximately 50 per cent in the manner described in the report of the work on phosgene. The outcome of this experiment is recorded in Table 90.

TABLE 90.—*The influence of oxygen upon dogs gassed with chlorine treated by the standard method*

	Treatment with oxygen		Treatment without oxygen (per cent)
	Number of dogs	Per cent	
Deaths in—			
24 hours.....	3	37.5	43
2 days.....	3	37.5	3
3 days.....	0	0	0
Total acute deaths.....	6	75	46
Delayed deaths.....	0	0	25
Recoveries.....	2	25	29
Survivals.....	2	25	54
Number of dogs.....	8		28

At this concentration of chlorine the toxicity series shows a percentage recovery of 9 per cent. The number of dogs involved in the present series was entirely too small to warrant a definite conclusion. The fact that the percentage of recoveries was increased by 16 per cent may be of significance. On the other hand, when comparison is made with treatment figures obtained, it is true, in a large number of dogs, it would appear that oxygen has little influence in increasing the number of recoveries; that is, with oxygen the recoveries were 25 per cent, without oxygen 29 per cent.

THE DETERMINATION OF OXYGEN CHANGES IN THE BLOOD OF GASSED DOGS BREATHING AIR IN COMPARISON WITH BREATHING OXYGEN

After it had been shown that oxygen administration alone or in combination with venesection was of doubtful value in reducing the mortality of dogs gassed with phosgene it was deemed important to determine the exact changes that occurred in the respiratory functions of the blood after exposure of animals to phosgene. Therefore the oxygen of the blood was determined in gassed dogs breathing air and breathing oxygen. As an ideal procedure for this purpose blood should be drawn from the right and left ventricles for the sample of venous and arterial blood, respectively, inasmuch as the blood contained in these receptacles undoubtedly more nearly represents the average composition than blood secured at a greater distance from the heart.

Although the figures may not be identical, the general results obtained by analysis of heart blood and that of vein and artery blood are of the same kind. This has been demonstrated. In the present investigation the venous blood was obtained by aspiration through a needle inserted through the skin into a jugular or femoral vein, and the blood drawn into a test tube under albolene. The arterial blood was obtained in the same way through a needle inserted through the skin into a femoral artery, the position of the artery being determined by palpation.

EXPERIMENTS WITH NORMAL ANIMALS

It was first ascertained whether the oxygen content of the arterial and venous blood of the normal dog can be raised by the administration of oxygen. As a result of these experiments (Table 91) it is quite evident that this was possible in those cases in which the arterial percentage saturation was low originally. It was not, however, an invariable rule.

TABLE 91.—*The arterial and venous oxygen content and percentage saturation breathing air as compared with breathing oxygen (approximately 50 per cent). The capacity of the blood (oxygen-combining power) is also given*

[Normal dogs]

Number	Capacity	Breathing air				Breathing oxygen			
		Arterial content	Venous content	Arterial percent-age saturation	Venous percent-age saturation	Arterial content	Venous content	Arterial percent-age saturation	Venous percent-age saturation
88	21.9	19.4	9.8	88	44.8	19.1	7.8	87.2	35.6
89	16.2	14.8	10.2	91	62.9	14.9	11.6	92.0	71.6
92	24.9	20.2	17.8	81	(?)71.5	21.9	15.5	88.0	62.2
99	15.9	16.0	9.4	100	59.8	15.8	8.2	99.4	51.5
101	17.7	15.8	9.2	89	(?)52.0	15.6	13.9	88.2	(?)78.5
102	18.0	16.4	11.5	91	63.8	16.4	11.4	91.2	63.4
103	15.7	12.4	-----	180	-----	14.3	-----	191.1	-----
104	18.6	17.3	9.3	93	50.0	18.4	13.3	98.0	72.0

¹ Died soon after gassing.

It should be noted that, in the cases where the percentage saturation of the venous blood showed a decrease while the dog was breathing oxygen as compared with the value obtained when the animal was breathing air, the contents did not vary by much more than 1.5 per cent. This was the error of the method used for analyzing oxygen (Henderson-Smith method).

EXPERIMENTS WITH GASED ANIMALS

The study of the blood oxygen was undertaken primarily to discover whether the determination of its content in the arterial and venous blood would not indicate the reason why oxygen alone seemed to have no therapeutic value, since, as has been noted above, the percentage of survivals in those series in which oxygen was given was practically identical with that obtained in the "toxicity series," for the same concentration of gas.

A study of Table 92 will show that in spite of the administration of oxygen and the ability of the animal to raise the oxygen content of the blood, in general, the percentage saturation became successively lower. In other words, although additional oxygen could in many cases be forced into the blood in relatively great amounts either soon after or several hours after gassing, nevertheless, owing to the gradual decrease of the oxygen content of the blood and the consequent lowering of the percentage saturation, the blood was further and further away from saturation.

TABLE 92.—*The influence of oxygen administration upon the percentage saturation and oxygen content of the blood of dogs gassed with phosgene (71 to 80 parts per million) (0.31 to 0.35 mgm. per liter)*

No.	Time	Capacity	Arterial content	Venous content	Arterial percentage saturation	Venous percentage saturation	Hemoglobin	Remarks
89	3.00	16.2	14.8	10.2	92.0	62.9	85	Normal; breathing air; July 17.
	4.00	16.2	14.9	11.6	92.0	71.6	80	Normal; breathing oxygen. Gassed, 8.39 a. m., July 18.
	10.30	15.1	15.4	-----	100.0	-----	85	Breathing air.
	1.15	16.1	14.9	7.1	92.0	48.0	80	Breathing air.
	2.30	17.4	16.6	-----	95.0	-----	85	Breathing oxygen.
	3.30	16.8	16.0	2.5	95.0	15.0	85	Breathing oxygen.
92	4.45	17.7	10.1	-----	57.0	-----	(?)	Breathing air.
	9.45	24.9	20.2	17.3	81.0	71.5	-----	Normal; breathing air; July 22.
	11.00	24.9	21.9	15.5	88.0	62.2	90	Normal; breathing oxygen. Gassed, 8.37 a. m., July 23.
	1.00	23.3	20.9	14.0	90.0	60.0	-----	Breathing air.
	4.00	27.5	28.7	20.3	100.0	73.0	140	Breathing oxygen.
	5.15	28.9	25.3	3.8	87.0	9.9	140	Breathing air.
95	10.30	18.7	17.4	8.4	93.0	45.0	85	Normal; breathing air; July 25. Gassed, 3.47 p. m., July 25.
	9.30	25.0	17.0	8.0	68.0	32.0	+100	Breathing air.
	11.00	25.0	20.3	9.6	81.0	38.0	110	Breathing oxygen.
	2.45	25.0	11.6	4.3	46.4	17.0	120	Breathing air.
	4.00	25.0	14.7	-----	59.0	-----	160	Breathing oxygen.
101	2.45	17.7	15.8	9.2	89.0	52.0	85	Normal; breathing air; July 29.
	3.45	17.7	15.6	13.9	88.2	78.5	90	Normal; breathing oxygen. Gassed, 9.20 a. m., July 30.
	10.45	12.8	12.2	4.1	95.0	32.0	-----	Breathing air.
	1.50	15.2	12.7	4.1	83.0	27.0	-----	Breathing air.
	3.20	21.6	14.3	4.9	66.0	22.0	120	Breathing oxygen.
	4.30	24.8	11.3	-----	46.0	-----	130	Breathing oxygen (died 5 p. m.).
104	2.50	18.6	17.3	9.3	93.0	50.0	75	Normal; breathing air; July 31.
	4.30	18.6	18.4	13.3	98.0	72.0	75	Normal; breathing oxygen. Gassed, 9.53 a. m., Aug. 1.
	2.00	18.0	15.4	-----	85.0	-----	65	Breathing air.
	3.45	21.6	15.0	-----	69.0	-----	90	Breathing air.
	5.40	21.7	12.3	-----	56.0	-----	56	Breathing oxygen (died 5.45 p. m.).
105	2.30	24.4	22.4	14.9	91.0	61.0	95	Normal; breathing air; Aug. 1. Gassed, 4.20 p. m., Aug. 1.
	9.30	27.1	25.1	9.4	93.0	34.0	140	Breathing air, Aug. 2.
	10.45	27.1	23.6	11.6	87.0	43.0	-----	Breathing oxygen.
	2.15	24.7	21.5	9.3	87.0	38.0	130	Breathing air.
	3.35	24.6	24.3	9.7	100.0	39.0	140	Breathing oxygen.
	4.20	24.6	24.5	-----	100.0	-----	-----	Breathing oxygen.
113	5.15	(?) 18.5	10.2	7.4	55.0	40.0	130	Breathing air.
	10.00	17.7	16.4	2.2	93.0	12.0	95	Breathing air, Aug. 3.
	9.00	15.6	14.8	5.1	95.0	32.0	90	Breathing air, Aug. 5.
	10.00	18.1	17.5	10.1	97.0	55.8	85	Normal; breathing air; Aug. 8. Gassed, 9.17 a. m., Aug. 9.
	1.00	24.5	22.4	6.6	91.0	27.0	130	Breathing air.
	3.00	27.0	28.9	2.6	100.0	9.9	140	Breathing oxygen.
	3.45	30.5	22.7	-----	74.0	-----	140	Breathing air (died 3.52 p. m.).

The hemoglobin values are only approximate, having been determined by the Talquist scale.

It was often observed that it was impossible to raise the venous content, although the arterial content could be markedly increased. This would seem to indicate that while there may have been an abundance of oxygen in the arterial blood for ordinary purposes, there was such an increased demand for it on the part of the tissues that the increased amount not only did not get to the venous blood, but the oxygen there might show a continued marked decrease. Dog No. 89 was an example of such a case, in which, although the oxygen in the arterial blood was increased, the percentage saturation being raised from 90 per cent to 95 per cent—the capacity showing relatively little change—it was impossible to prevent a very rapid fall in the oxygen content of the venous blood. As long as the dog was breathing oxygen the arterial per-

centage saturation remained high, but fell off rapidly when atmospheric air was substituted for the 50 per cent oxygen. Dog No. 113 exemplified a similar condition.

Speaking of the "capacity" is perhaps applying a misnomer for the condition which we had in these gassed dogs. That is, the term did not here represent the true combining power of the blood, in the body, with oxygen, in the conditions where the blood had thickened considerably. A cubic centimeter of thickened blood contained more hemoglobin, in ratio to the plasma, than did a cubic centimeter of blood of normal or average viscosity. In the body the capacity of the blood as a whole must be really lower, since it has lost in volume, due to the loss of water. This probably explains, in part, the drop in oxygen content. Furthermore, the increased viscosity slowed the blood stream, and led to poor oxygenation of the tissues.

Dog No. 105, an animal that recovered, illustrates a recovery which was plainly not due to the oxygen. Seventeen hours after gassing the percentage saturation of the arterial blood was practically the same as the normal figure (93 per cent as compared with 91 per cent). The arterial content rose parallel with the capacity, the former increasing from 22.4 to 25.1, the latter from 24.4 to 27.1.

The venous content, on the other hand, had dropped from 61 per cent to 23 per cent. Oddly enough, when the blood was examined after the dog had been breathing oxygen, the arterial content was found to be lower, while the venous content was higher. This was obviously a mistake in the one or the other analysis. But it is interesting to note that the next arterial sample, taken at 2.15, had a lower oxygen content still, although the percentage saturation was the same as the oxygen breathing sample, due to a gradual fall in the capacity; and that the sample of venous blood when the dog was breathing air had about the same content as a previous sample taken when the dog was breathing air at 9.30. Be that as it may, the next administration of oxygen, beginning at 2.20, raised the arterial content to 100 per cent saturation, although the capacity was decreasing all the time, and kept it raised while the oxygen of the venous blood seemed to have been prevented merely from decreasing. There was a sharp falling off of the oxygen in the arterial blood, the saturation dropping to 55 per cent, after the dog was returned to air, and a drop in the capacity, which had the effect of raising the saturation of the venous blood, although the venous content was actually lower. The later figures show the condition 41 to 65 hours after gassing, respectively. The capacity decreased still further, below normal, and at 41 hours after gassing the venous saturation dropped as low as 12 per cent, although the arterial was practically normal (93 per cent). Sixty-five hours after gassing the venous percentage saturation had risen to 32 per cent, or about the value for it 17 hours after gassing, but only about one-half that of normal.

Dog No. 113 showed in summary fashion the inefficiency of oxygen as a therapeutic agent alone, in a crucial case, that is, one in which the effects of the poison were advancing rapidly. This case showed as marked and as rapid a rise in the "capacity," or of the thickening of the blood, as any that have

come under our observation. The arterial content rose with the capacity, but not fast enough to keep up the percentage saturation, which dropped from 97 per cent to 91 per cent four hours after gassing. The venous blood lost oxygen. Oxygen administration was begun at the fifth hour after gassing. The percentage saturation of the arterial blood six hours after gassing was 100 per cent; the venous continued to fall rapidly. Forty-five minutes later, although still breathing oxygen, the percentage saturation had fallen to 74 per cent, while there was no oxygen that could be detected in the venous blood. The content of the arterial blood at this time was the same as its value four hours after gassing while the dog was breathing air. But the capacity was then 30.5 as compared with 24.5 four hours after gassing. Another sample taken five minutes later, the dog having been returned to air, showed a still further decrease in oxygen content of the arterial blood, and a few minutes later the dog died.

This was particularly important as illustrating the futility of dealing directly with one of the secondary effects of gas poisoning, viz, the reduced amount of oxygen in the tissues. The lack of oxygen must be in one of two places, either in the arterial blood, because it can not be taken up from the lungs; or, if the arterial blood can take up oxygen in additional amount, the lack of oxygen is in the tissues themselves. The first possibility is ruled out, inasmuch as oxygen can be absorbed by the gassed lungs. In spite of the fact that the oxygen of arterial blood may be within normal limits under oxygen administration there still may be evident oxygen want in the tissues. Obviously oxygen administration alone does not eliminate the crucial condition in gas poisoning, namely, lack of oxygen in the tissues. Although an additional amount of oxygen in the inspired air may be of some benefit to the tissues, the primary object in treatment should be to remove or modify the cause for the lack of oxygen.

Although oxygen could not be shown to have a curative effect on dogs gassed at the "lethal" concentration (viz, 70 to 80 parts of phosgene per million of air; 0.30 to 0.35 mgm. per liter), the question was raised as to whether it would be beneficial to animals gassed at a lower concentration, and perhaps thus more in accord with conditions of men in the trenches. Accordingly the study of the oxygen in the blood of dogs gassed at a concentration of 50 to 60 parts phosgene (0.21 to 0.26 mgm. per liter) was made. Table 93 is a summary of the results. From these data the same general conclusions may be drawn regarding dogs gassed with a concentration of phosgene lower than lethal as pertained to dogs gassed at 70 to 80 (0.30 to 0.35 mgm. per liter). In some cases it was impossible to raise the venous content (dog No. 126), although this was exceptional. In others, after an initial raising of the percentage saturation of both arterial and venous blood, there was a more or less rapid fall even while the animal was breathing oxygen, which became more rapid after a return to breathing air (e. g., dogs Nos. 123 and 124).

No.	Time	Capacity	Arterial content	Venous content	Arterial percent-age saturation	Venous percent-age saturation	Hemo-globin	Remarks
116	11.00	20.8	17.8	12.0	85.0	57.6	90	Normal; breathing air; Aug. 12. Gassed
	9.00	23.8	20.7	7.3	87.0	30.7	150	3.10 p. m., Aug. 12.
	10.00	23.2	21.3	6.4	92.0	27.6	170	Breathing air, Aug. 13.
	11.00	22.5	19.9	7.4	88.0	32.9	120(?)	Breathing oxygen.
	2.30	22.5	17.9	5.4	79.0	24.0	130	Breathing air.
	3.45	22.0	18.4	10.0	83.0	45.4	130	Breathing oxygen.
	4.30	20.2	16.6	5.9	82.0	29.0	140	Breathing oxygen.
118	1.15	25.3	23.0	17.6	91.0	69.6	90	Normal; breathing air; Aug. 12. Gassed,
	9.10	29.1	25.4	10.0	87.0	34.3	130	2.16 p. m., Aug. 13.
	10.10	27.6	25.7	15.7(?)	83.0	57.0	140	Breathing air, Aug. 14.
	11.15	27.6	25.5	11.4	83.0	41.3	140	Breathing oxygen.
	12.00	27.7	7.0	2.9	25.0	10.4	140	Breathing air.
	3.00	24.8(?)	18.4	3.1	74.0	12.7	140	Breathing air.
	4.00	27.9	23.4	7.3	84.0	26.1	140	Breathing oxygen.
	4.15	27.9	10.9		39.0		140	Breathing air.
121	9.00	10.9	9.5	4.3	87.0	39.7	80	Normal; breathing air; Aug. 15.
	12.00	10.1	9.1	2.9	90.0	28.7	80	Normal, breathing air, Aug. 15. Gassed,
	2.30	14.6	7.5	0.7(?)	51.0	4.7	90	8.59 a. m., Aug. 16.
	3.35	14.0	10.9	3.0	78.0	21.4	80	Breathing air.
	4.20	14.8	11.9	1.3	81.0	8.8	80	Breathing oxygen.
	4.30	14.8	2.9		24.0			Breathing air
123	11.30	14.9	13.7	2.5	92.0	17.8	80	Normal; breathing air; Aug. 16. Gassed,
	9.00	18.3	15.4	1.7	84.0	9.3	140	3.57 p. m., Aug. 16.
	9.45	20.3	17.6	2.6	86.0	12.8	150	Breathing air, Aug. 17.
	11.00	20.3	15.2	1.5	74.0	7.4	145	Breathing oxygen.
	11.30	20.3	6.8		33.0		145	Breathing air.
126	9.15	18.0	16.7	10.0	92.7	55.5	90	Normal; breathing air; Aug. 19. Gassed,
	11.25	24.7	23.8	12.1	96.3	49.0	135	2.13 p. m., Aug. 20.
	12.00	21.4	21.0(?)	10.7	100.0	45.8	135	Breathing air, Aug. 21.
	12.23	24.0	24.2		100.0		135	Breathing oxygen.
	12.49	24.0	23.7	10.2	99.0	42.0	130	Breathing oxygen.
	1.05	24.0	21.2		88.0		130	Breathing air.
	10.15	21.9	19.1	8.4	82.6	38.3	110	Breathing air, Aug. 22.
131	11.40	21.6	13.2	12.0	61.1	55.5	120	Normal; breathing air; Aug. 22. Gassed,
	11.45	17.9	17.5	8.0	97.7	44.6	120	9.52 a. m., Aug. 23.
	2.45	20.7	19.6	8.2	94.8	40.0	120	Breathing air.
	3.20	20.5	19.2	8.3	93.6	41.2	120	Breathing air.
	3.45	20.2	21.3	11.7	100.0	57.9	120	Breathing oxygen.
	4.10	20.5	20.5		100.0		120	Breathing oxygen.
	4.35	23.3	20.2	13.1(?)	86.7	56.2	120	Breathing air.
	12.00	23.7	20.4	2.5	86.0	10.5	120	Breathing air, Aug. 24
134	10.30	21.3	20.9	8.4	93.0	39.0	100	Normal; breathing air; Aug. 26. Gassed,
	8.45	27.5	14.6	7.3	53.0	27.0		11 a. m., Aug. 26.
	9.20	27.0	23.2	8.0	85.0	29.0	120	Breathing air, Aug. 27.
	9.50	26.4	20.9	12.1	79.0	45.0	140	Breathing oxygen.
	10.25	26.0	19.9	10.7	76.0	41.		

THE INFLUENCE OF VENESECTION AND INFUSION UPON OXYGEN CHANGES
IN THE BLOOD DURING OXYGEN ADMINISTRATION

It is apparent from the study of the blood oxygen as outlined above that oxygen alone can not be of more than temporary value in relieving the effects of gas poisoning. The next logical step in the development of the possible therapeutic use of oxygen was the study of the blood following bleeding and infusion plus oxygen administration. A large number of experiments were carried through. From the results of the experiments on the dogs which were placed in the oxygen chamber after venesection it is clearly evident that the respiratory function of the blood was not improved by venesection alone. Although no study of the influence of venesection on the arterial and venous content of the blood was made immediately after venesection, data are available which show that the beneficial effects of breathing oxygen instead of air are considerable, although practically the same as the effects obtained when venesection is not performed. From these data it is quite evident that bleeding does not materially alter conditions relative to the respiratory functions of the blood. However, at the time of venesection the oxygenation of the blood and tissues is not, in general, markedly deficient. The respiratory function of the blood is distinctly better when an animal is breathing oxygen than when ordinary air is breathed. The order of change is not, however, appreciably different from that which obtains when an animal breathes oxygen without venesection.

Bleeding followed by infusion may be said to have a decidedly beneficial effect upon the oxygenation of the blood. This is indicated by the fact that even when an animal is breathing air the venous blood carries more oxygen, which may be interpreted to mean that the tissues are being better supplied with oxygen. Oxygen administration at this time results, in general, in restoring the arterial blood to limits near the normal and in raising appreciably the venous saturation. It would appear that bleeding plus infusion so changes the physical character of the blood as to render possible a more complete oxygenation of tissues. The interpretation placed upon these results is that infusion decreases the viscosity of the blood, at least temporarily, so that capillary circulation is improved and, as a consequence, more adequate tissue respiration is possible. The dissociation of the oxyhemoglobin is probably also increased in accordance with the result of Barcroft on the effect of electrolytes on the dissociation curve of hemoglobin. It seems, therefore, that the optimum conditions for the use of oxygen are in connection with bleeding and infusion of salt solution. No single procedure is adequate; a combination of the three approaches the optimum treatment.

THE INFLUENCE OF GASSING AND TREATMENT UPON THE VOLUME OF
AIR BREATHED AND UPON THE PULSE

The extent of oxygenation of the blood will depend directly upon the rate of respiration and the volume of air breathed per minute and upon the circulation rate through the lungs. It becomes of importance, therefore, to determine these factors if a complete knowledge is desired concerning changes induced by gassing. Owing to insurmountable obstacles the circulation rate could not be determined in this investigation. The volume of air breathed and the respiration rate, however, have been followed in a measure and the observa-

tions indicated that shortly after gassing the respiration was markedly increased but that the volume of air breathed per minute was slightly less than normal. In other words, there was present rapid shallow breathing and undoubtedly less air, hence oxygen was in contact with blood in the lungs during a given period on the assumption that the circulation rate was constant.

Bleeding had no noticeable influence upon either the rate of respiration or the volume of air breathed per minute. Infusion, however, caused a rapid increase in both. Oxygen administered did not exert a marked influence in either particular.

The pulse rate was distinctly decreased soon after gassing but gradually increased to a maximum several hours later. If oxygen was administered during the period of the increasing heart beat, only a slight decrease in the rate was to be noted.

RESPIRATORY EXCHANGE

From data collected in the study of the respiratory exchange it may be said that both oxygen consumption and carbon dioxide production were distinctly lowered by exposure to phosgene. Breathing oxygen under these circumstances increased the oxygen consumption. In general, oxygen administration increased the carbon-dioxide production to a slight degree.

Bleeding caused a slight increase in oxygen consumption, although still below normal.

Infusion raised the oxygen consumption and, in general, the carbon-dioxide production. Oxygen administration after infusion brought the oxygen consumption back to the normal level and might indeed carry it above. This should be considered in connection with the percentage saturation of arterial and venous blood. As has been pointed out above, the venous blood carried more oxygen after infusion than before. The administration of oxygen after infusion resulted practically in complete saturation of the arterial blood as well. The oxygen consumption was equal to or greater than normal, while the arterial blood was almost completely saturated, and the venous percentage saturation indicated that the tissues were getting an ample supply of oxygen.

The conclusion is warranted, therefore, that the method of treatment involving venesection, infusion, and oxygen administration is indicated for the reestablishment of normal conditions in the respiratory functions of the blood in an animal gassed with phosgene. It should be emphasized that oxygen administered alone is entirely inadequate to combat the effects of phosgene poisoning inasmuch as this procedure does not eliminate the primary cause, namely, the concentration of blood. When treatment succeeds in restoring blood concentration to a more nearly normal level oxygen administration is of decided benefit.

CHAPTER XX

THE INFLUENCE OF OXYGEN ADMINISTRATION ON THE CONCENTRATION OF THE BLOOD WHICH ACCOMPANIES THE DEVELOPMENT OF LUNG EDEMA ^a

The enormous and rapid development of edema of the lungs which results from severe gassing of animals with the lung irritants used in warfare offers an unusual opportunity for studying the physiological effects accompanying this pathological condition. The rapidity with which the edema develops precludes the possibility of infection complicating the symptoms observed, and the condition which may develop after exposure to high concentrations of poisonous gas is so severe that the correlated symptoms can hardly be overlooked.

Loss of water from the blood is one of the most characteristic phenomena accompanying the development of edema of the lungs in animals gassed with lung irritants. A concentration of the blood becomes evident at about the time when the edema of the lungs can be first demonstrated. Thereafter the loss of water from the blood and the increase in severity of the edema run roughly parallel. The conclusion was made, therefore, that the two are inter-related and that the pouring of water into the lungs is the cause of the concentration of the blood.

Other considerations, however, make it necessary to proceed with caution before accepting this hypothesis. During the acute period after gassing there develops a deficiency of oxygen carried by the blood. Probably due to the poor aeration of the blood in the damaged lung the oxygen content of arterial and venous blood may drop to levels much below normal. The transport of oxygen to the tissues may be still further reduced by the decreased rate of blood flow, with the probable result that the oxygenation of the tissues is seriously interfered with.

Physiologists have shown that muscle tissue imbibes water when supplied with insufficient oxygen. Based on this observation, the hypothesis may be presented that the concentration of the blood is due not primarily to the development of lung edema but to the imbibition of water from the blood by the tissues which are not sufficiently oxygenated. To throw some light on the validity of this hypothesis the experiments reported below were carried out.

Goats were gassed with lethal concentrations of chloropicrin. As soon as possible after gassing, half of the animals were fitted with masks and given oxygen continuously in known quantities by means of a Haldane oxygen apparatus.^b The other animals were used as controls.

The hemoglobin content was used as an index of the concentration of the blood. Hemoglobin determinations were made frequently, using blood obtained by pricking an ear vein. Blood from the heart punctures was also used. The Haldane method was used for the hemoglobin determinations.

^a This chapter, which deals with the experimental observations of Capt. D. W. Wilson, C. W. S., and Capt. S. Goldschmidt, C. W. S., made in the physiological laboratories of the Royal Engineers Experimental Station, Porton, England, is reprinted in full from the *American Journal of Physiology*, Baltimore, 1919, No. 1, 157-164.

^b The Haldane oxygen apparatus furnishes oxygen to a mask fitted with valves for incoming and outgoing air. When the mask is worn by the animal, breathing is easy and the air in the mask may be enriched by varying amounts of oxygen.

When the concentration of the blood was sufficiently marked in the animals to which oxygen was being administered, heart punctures were made and the percentage saturation of the hemoglobin of the bloods from the right and left hearts was determined by means of Barcroft's differential blood gas apparatus.^c Some difficulty was experienced in obtaining blood from the hearts of animals in which the lungs were large and edematous, but the sample was considered satisfactory when it was obtained quickly and with little struggling on the part of the animal.

The following protocols give the results obtained in this series of experiments:

Animals gassed with chloropicrin 1 to 8,500 for 25 minutes (10.10 to 10.35 a. m.), August 19, 1918

GOAT 4537

9.35 a. m. Hb. 80.
10.35 a. m. Gassed.
11 a. m. Continuous oxygen by mask, 1 liter per minute.
11.40 a. m. Hb. 79 (100 per cent).
2.20 p. m. Hb. 85 (106 per cent).
2.45 p. m. Continuous oxygen by mask, 3 liters per minute.
4.25 p. m. Hb. 105 (131 per cent).
4.45 p. m. Heart puncture. Arterial blood 93 per cent saturated. Venous blood 45 per cent saturated.
5.45 p. m. Hb. 110 (137 per cent).
5.55 p. m. Died. L : H 8.2.

GOAT 4406 (CONTROL)

9.45 a. m. Hb. 42.
10.35 a. m. Gassed.
12.10 p. m. Hb. 48 (114 per cent).
2.30 p. m. Hb. 60 (143 per cent).
3 p. m. Died. L : H 6. 0

GOAT 4567

10 a. m. Hb. 60.
10.35 a. m. Gassed.
11 a. m. Continuous oxygen by mask, 1 liter per minute.
11.50 a. m. Hb. 70 (117 per cent).
2.40 p. m. Hb. 84 (140 per cent).
2.45 p. m. Continuous oxygen by mask, 3 liters per minute.
3.45 p. m. Hb. 105 (175 per cent). Heart puncture. Venous blood 55 per cent saturated. Animal died on table. L : H 8.0.

GOAT 4542 (CONTROL)

9.50 a. m. Hb. 74.
10.35 a. m. Gassed.
12.20 p. m. Hb. 76 (103 per cent).
2.50 p. m. Hb. 88 (119 per cent).
5.30 p. m. Hb. 96 (130 per cent). Found dead next morning. L : H 8.3.

Animals gassed with chloropicrin 1 to 8,500 for 30 minutes (9.30 to 10 a. m.), August 21, 1918

GOAT 4526

5.35 p. m. (Aug. 19.) Hb. 53.
10 a. m. Gassed.
10.15 a. m. Continuous oxygen by mask, 1½ liters per minute.
12 m. Hb. 67 (126 per cent).
12.15 p. m. Continuous oxygen by mask, 4 liters per minute.
2.10 p. m. Hb. 70 (132 per cent).
3.20 p. m. Hb. 73 (138 per cent).
3.50 p. m. Hb. 76 (143 per cent). Heart puncture. Arterial blood 90 per cent saturated. Venous blood (obtained only after struggling) 20 per cent saturated.

GOAT 4526—Continued

4.15 p. m. Oxygen stopped.
5.30 p. m. Hb. 76 (143 per cent).
6.05 p. m. Died. L : H 7.7.

GOAT 4446 (CONTROL)

5.30 p. m. (Aug. 19.) Hb. 72.
10 a. m. Gassed.
12.15 p. m. Hb. 96 (133 per cent).
1.45 p. m. Hb. 118 (164 per cent).
2 p. m. Died.

^c We are indebted to Mr. Barcroft, Captain Dunn, and Captain Peters for these data.

*Animals gassed with chloropicrin 1 to 8,500 for 25 minutes (9.16 to 9.41 a. m.)
August 23, 1918*

GOAT 4577

5.50 p. m. (Aug. 22.) Hb. 60.
9.41 a. m. Gassed.
9.55 a. m. Continuous oxygen by mask, 3
liters per minute.
10.23 a. m. Hb. 70 (117 per cent).
12.12 p. m. Hb. 81 (135 per cent).
2.35 p. m. Hb. 95 (158 per cent). Heart
puncture. Both samples obtained only
after struggling. Arterial blood 58 per
cent saturated. Venous blood 4 per cent
saturated.
2.40 p. m. Died on table. L : H 7.4.

GOAT 4490 (CONTROL)

9.41 a. m. Gassed.
10.43 a. m. Hb. 85.
12.30 p. m. Hb. 100 (118 per cent).
2.15 p. m. Hb. 124 (146 per cent).
2.20 p. m. Died. L : H 6.7.

GOAT 4631

5.45 p. m. (Aug. 22.) Hb. 58
9.41 a. m. Gassed.
9.55 a. m. Continuous oxygen by mask, 3
liters per minute.
10.10 a. m. Hb. 54 (93 per cent).
12 m. Hb. 58 (100 per cent).
2.50 p. m. Hb. 61 (105 per cent).
5 p. m. Hb. 67 (116 per cent).
5.55 p. m. Hb. 69 (119 per cent).
6.20 p. m. Heart puncture. Arterial blood
95 per cent saturated. Venous blood
about 50 to 60 per cent.
6.20 p. m. Hb. 74 (128 per cent). Died on
table. L : H 5.7.

GOAT 4457 (CONTROL)

9.41 a. m. Gassed.
10.54 a. m. Hb. 94.
12.20 p. m. Hb. 96 (102 per cent).
3.15 p. m. Hb. 106 (113 per cent).
6.30 p. m. Hb. 124 (132 per cent). Found
dead next morning. L : H 7.1.

Curves showing the concentration of the blood are reproduced in Charts XXIX, XXX, XXXI. In the charts, the percentage variations from the normal are plotted to make all of the curves directly comparable.

The maximum concentrations observed in the control animals varied from 30 per cent to 60 per cent above normal (average 43 per cent), while in the animals receiving oxygen the variation was from 28 per cent to 75 per cent above normal (average 48 per cent). It is apparent that, on the whole, the blood of animals which received oxygen concentrated as rapidly and to as great an extent as that of the control animals.

In order to demonstrate the efficiency of the oxygen administration, samples of blood were taken from both sides of the heart at suitable intervals and analyzed for oxygen. In most of the experiments the venous and arterial blood samples were obtained from the heart without difficulty and contained hemoglobin which was normally saturated with oxygen. With the increased concentration of the hemoglobin the oxygen content of the blood was even above normal.

Occasionally the blood was obtained only after considerable struggling on the part of the animal, so that the reduced oxygen content of such bloods was to be expected. These observations are reported here merely to make the experimental record complete, as obviously the low oxygen content of such bloods is without bearing on the present problem.

These experiments demonstrated that, by breathing oxygen-rich atmospheres, oxygen could be absorbed through the damaged and edematous lungs in quantities sufficient to maintain a practically normal level of oxygen in the arterial blood. The high saturation of the hemoglobin of venous blood with oxy-

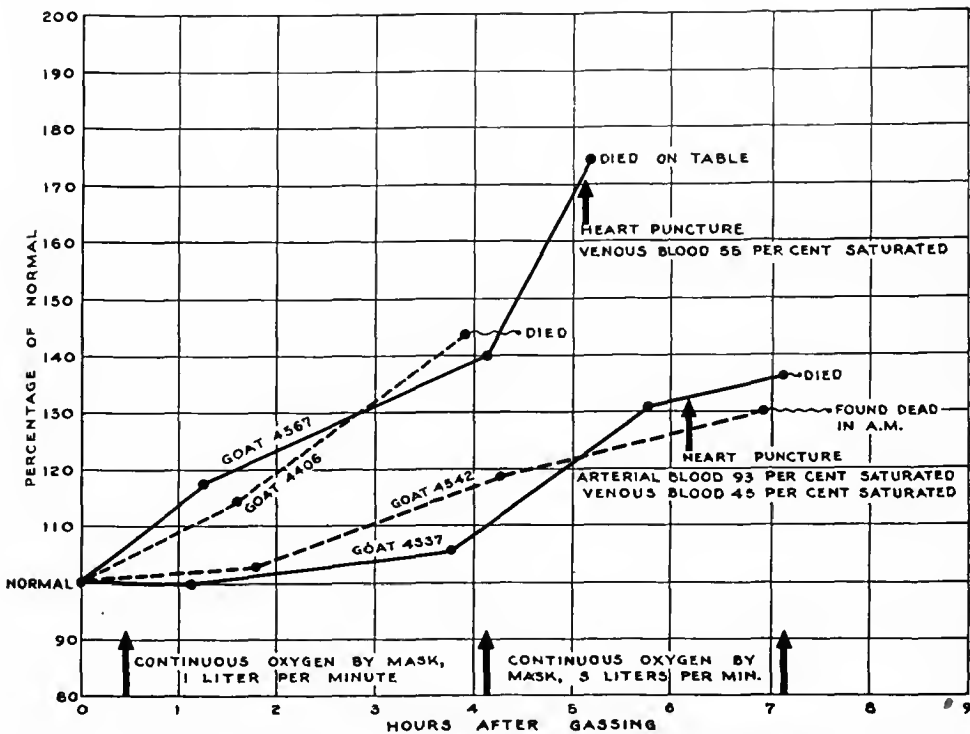


CHART XXIX.—Changes in hemoglobin of the blood after gassing with chloropierin 1/8500 for twenty-five minutes. Solid line: Animals receiving extra oxygen. Broken line: Control animals

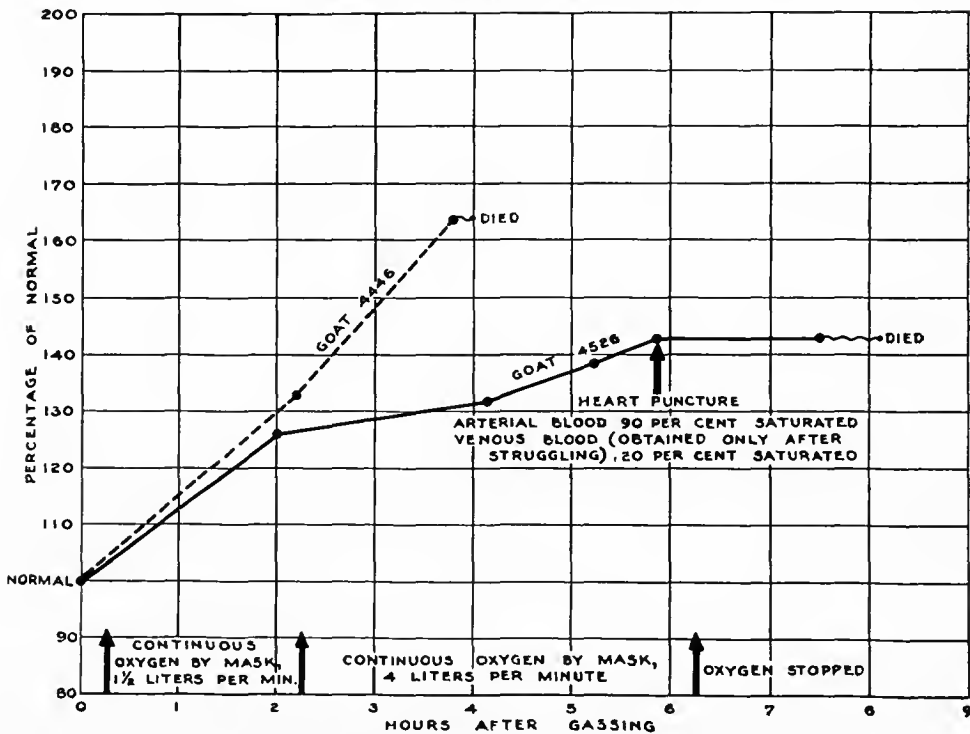


CHART XXX.—Changes in hemoglobin of the blood after gassing with chloropierin 1/8500 for thirty minutes. Solid line: Animal receiving extra oxygen. Broken line: Control animal

gen would seem to prove that the blood flow was sufficiently rapid to normally oxygenate the tissues. Nevertheless, in spite of the normal oxygenation of the tissues in the animals receiving oxygen, the blood concentrated as rapidly and to as great an extent as in the control animals. The conclusion therefore seems justifiable that the lack of oxygen in the tissues and consequent imbibition of water is not an important factor in causing the concentration of the blood in animals developing edema after being gassed with lung irritants.

An indication of the severity of the lung edema was obtained by comparing the weight of the lung to the weight of the heart at autopsy. The high lung to heart ratios obtained in practically all of the animals studied show that a severe grade of edema had already developed. The extent of the edema as indicated by this method was as great in the animals receiving oxygen as in the

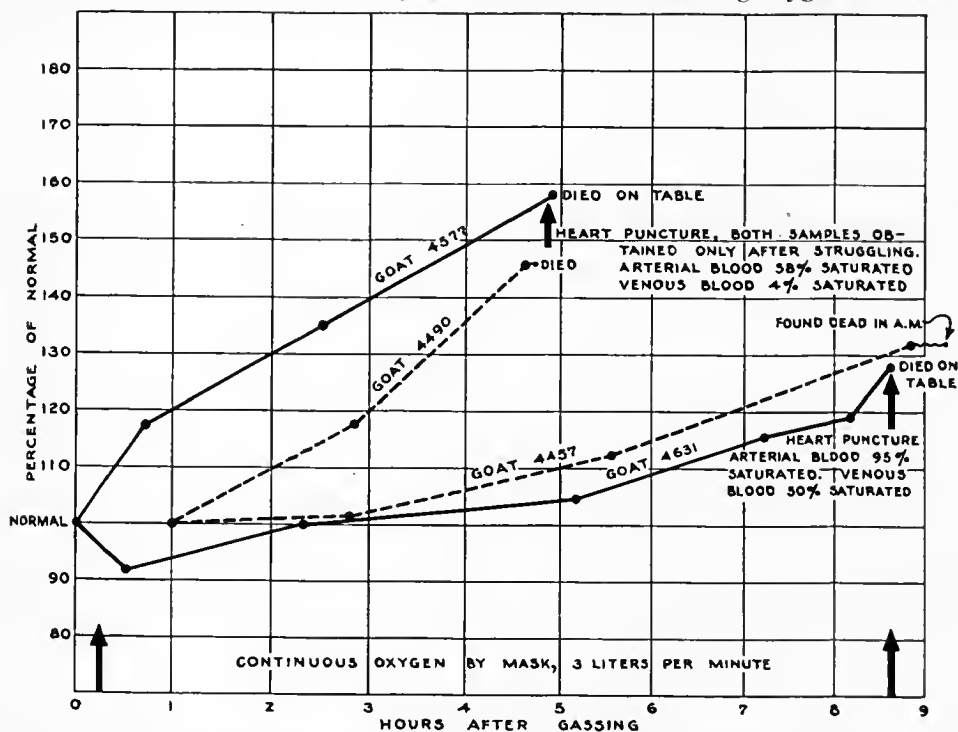


CHART XXXI.—Changes in hemoglobin of the blood after gassing with chloropirin 1/8500 for twenty-five minutes. Solid line: Animals receiving extra oxygen. Broken line: Control animals

controls. Although the data are necessarily few, it is apparent that the efficient oxygenation of the lung tissue in the animals receiving oxygen failed to diminish the tendency for the development of the edema of the lungs.

With the enormous accumulation of fluid in the edematous lungs and the loss of water from the blood running roughly parallel, it is a tempting study to estimate even in a rough way the possible water interchange. An attempt has been made with data which are more or less incomplete and with calculations involving gross errors but the relations are so striking that they are presented in Table 94. In this table are recorded data and calculations from animals in which the hemoglobin was not determined immediately before death but is estimated from the curve obtained from the various determinations. These estimated values are quite similar to average values obtained at death on other animals.

TABLE 94.—*Comparison of calculated amounts of fluid lost from blood and extra fluid in the lungs of gassed animals*

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)
Goat No.	Date	Weight animal	Weight heart at death	Weight lung at death	L.H.	Weight normal lung	Last hemoglobin determination	Hemoglobin at death	Normal blood volume	Blood volume at death	Fluid lost from blood at death	Extra fluid in lung
		<i>Kgm.</i>	<i>Grams</i>	<i>Grams</i>		<i>Grams</i>	<i>Per cent</i>	<i>Per cent</i>	<i>C. c.</i>	<i>C. c.</i>	<i>C. c.</i>	<i>C. c.</i>
3602-----	June 13	31.8	157	1,472	9.4	377	163	200	1,750	875	875	1,095
3638-----	June 12	29.5	126	623	4.9	302	125	140	1,625	1,160	465	321
3787-----	June 20	16.8	74	566	7.6	178	128	145	925	638	287	388
4098-----	July 4	35.0	195	1,103	5.7	468	114	140	1,925	1,375	550	635
4406-----	Aug. 19	15.5	85	510	6.0	204	143	150	850	567	283	306
3920-----	July 4	37.8	200	1,700	8.5	480	180	(1)	2,080	1,155	925	1,220
3600-----	June 12	25.5	130	849	6.5	312	154	(1)	1,400	910	490	537
4047-----	July 12	33.6	210	1,556	7.4	504	103	(1)	1,850	1,420	430	1,052

Column 6=column 5 ÷ column 4.

Column 7=column 4 × 2.4.

Columns 8 and 9. Values calculated using the normal as 100 per cent.

Column 9=extrapolation to time of death.

Column 10=column 3 × 0.055 × 1000 (Boycott and Damant, Journ. Physiol., 1907-8, xiv, 36).

Column 11=column 10 ÷ column 9.

Column 12=column 10 — column 11.

Column 13=column 5 — column 7.

¹ Time of death not known. Calculations made using last hemoglobin determinations (column 8).

Examining the last two columns of the table it is evident that in only one instance the amount of extra fluid in the lung was less than the calculated loss of fluid from the blood. In some instances the extra fluid in the lung was much greater than that lost by the blood. Little or no water was drunk by goats in this condition and the volume of urine excreted was small, so that the external factors did not confuse the picture. Even with the relatively large errors of calculation involved, the conclusion seems justified that the loss of fluid by the blood could be accounted for by the excess of liquid in the edematous lung.

The evidence suggests that the muscles, etc., do not imbibe water and cause the concentration of the blood. In fact it would appear that water may be drawn from some tissues to make up part of the volume of liquid in the lung. One is thus finally led back to the original point of view that the development of the edema of the lungs and the concentration of the blood are interrelated, and are the important factors in the pathological condition studied. With this fact established it is justifiable to conclude that the development of the edema of the lungs is the primary factor in the condition and that the development of the edema causes the concentration of the blood.

SUMMARY

The continuous administration of oxygen to goats gassed with chloropicrin did not inhibit the concentration of the blood.

The percentage saturation of the hemoglobin with oxygen was normal even after a considerable concentration of the blood had occurred.

The concentration of the blood is not caused by the inhibition of water by the tissues as the result of oxygen want.

The loss of water from the blood is therefore due to the development of the edema of the lungs.

CHAPTER XXI

RESEARCHES OF THE PATHOLOGICAL AND PHYSIOLOGICAL SECTIONS, HANLON FIELD (EXPERIMENTAL GAS FIELD^a)

INTRODUCTION

A brief outline of the organization, location, and scope of work of the experimental gas field, known as Hanlon Field, is given in Chapter II. Of the sections of the field, only the medical sections (pathological and physiological sections) come within the scope of the present volume.

Personnel detailed from the Medical Corps had been attached to the staff of the field, and had acted in an advisory capacity from a very early date. Yet, because of the technical nature of the equipment required and the consequent difficulty in obtaining it, the medical sections were practically the last to come into active operation at the field. Nevertheless, very detailed and extensive work was under way and completed in some parts at the time of the armistice.

This work had been separated and designated under the heads of the pathological section and physiological section. However, the total quantity of material collected to the close of the field was not of such volume as to make necessary a separate summary report under each section. Accordingly, the whole is considered here under one head, no effort being made to indicate the particular work done under the direction of the personnel of each section. In fact, the actual experiments were closely interrelated and were made with such cooperation that it would have been difficult to make such a separation in any case.

A very considerable part of the work which these sections were able to do was concerned with the study of the lesions produced by various vesicants, or of internal toxic effects produced by "gases" taken into the body of animals or man either through the respiratory organs or by intravenous injection. A number of these investigations were carried out by these sections solely to determine the pathological effects produced by various war gases for the sake of the data alone. Such studies were embodied in the reports of these sections

(^a) This chapter comprises the full text of a special Summary Report of the Work of Hanlon Field (Experimental Gas Field), Chemical Warfare Service, American Expeditionary Forces, France, pathological and physiological sections, with certain changes in the arrangement.

The following special reports which were submitted, through military channels, to the Chief, Chemical Warfare Service, are included in this chapter:

Special Report No. 39: Effects of Intravenous Injections of Dichlorethylsulphide in Rabbits, with Special Reference to the Blood and Hematopoietic Tissues. Submitted by Maj. A. M. Pappenheimer, M. C., and Capt. Morgao Vance, M. C., November 10, 1918.

Special Report No. 38: The Cutaneous Lesions Caused by Dichlorethylsulphide and Lewisite in the Horse. Submitted by Maj. A. M. Pappenheimer, M. C., November 2, 1918.

Special Report No. 57: Toxicity of Dimethyltrithiocarbonate. Submitted by Maj. A. M. Pappenheimer, M. C., for Maj. H. C. Clark, M. C. The work was performed by Capt. S. Goldschmidt, M. C.; Capt. B. M. Vance, M. C.; and Capt. D. W. Wilson, M. C., November 29, 1918.

Special Report No. 15: The Behavior of Certain Slugs and Snails in the Presence of Dichlorethylsulphide (IIS) Submitted by Maj. H. C. Clark, M. C., in charge of the pathological section, August 20, 1918.

Special Report No. 44: A Suit Designed by Capt. H. G. Knowland, C. W. S., and Second Lieut. T. M. Knowland, C. W. S., for protection against Mustard Gas. Submitted by Maj. A. N. Richards, S. C.; Capt. S. Goldschmidt, C. W. S.; and Capt. H. G. Knowland, C. W. S.; November 18, 1918.

Special Report No. 49: The Protective Power of Sag Paste, Calcium Hypochlorite Ointment, and Petrolatum against Dichlorethylsulphide (IIS) and Lewisite I. Submitted by Maj. C. B. Kerr, M. C., November 26, 1918.

and covered specifically three compounds, namely, dichlorethylsulphide or mustard gas, Lewisite I, and dimethyltrithiocarbonate. In addition, a very large number of examinations of lesions and general body conditions were made as autopsies in the cases of animals "gassed" in course of general field experiments carried out in cooperation with other sections. Such examinations became of the nature of routine for these sections, and results from them were given in general in the reports covering the main experiments, hence issued by other sections, in particular, the field gas experimentation section.

The second phase of the work done by the medical sections was the study of various methods of gas defense through the medium of physiological tests. No work on masks, however, was included under this function. On the other hand, because of the great importance which mustard gas had acquired in operations, these studies were concerned almost entirely with defense against this vesicant. These investigations took up, first, certain methods of the detection or estimation of the strength of air concentration of mustard gas. The proposal, originating at the American University, to use the behavior of snails for the detection of mustard gas was considered. Other low-form organisms were also tested for the same characteristics. At the same time, an attempt was made to standardize for rapid estimations the relation between the concentration of mustard gas in the air mixture and degree of lesion produced on human skin. In addition to the work on the detection of mustard gas, several investigations were carried out on special equipment for protection against this gas. These comprised tests of treated fabrics, various skin ointments, of which "sag paste" is the best example, and "tar" materials for the protection of horses' feet. Finally, in the study of mustard-gas defense the general problem of the treatment of lesions produced by the same gas had been taken in hand. As is well known, no effective solution of this important problem was ever reached, either by our own service, or that of our Allies or of the enemy.

A third phase of the activities of these sections was the observation of actual gas casualty cases in hospitals, and the collection and examination of specimens from autopsies.^b This work was taken in hand quite late and never fully developed. This function of the medical services in the field would certainly have been extended had the war continued.

TOXICITY AND VESICANT TESTS

MUSTARD GAS

Two studies were made directly for determining the effects produced by dichlorethylsulphide, each concerning a rather special and hitherto untouched phase of the general question of mustard gas pathology.

The first of these was a short investigation to determine the accuracy of the conclusion arrived at in some experiments that the serum from mustard-gas blisters was capable itself of a vesicant action. Twenty human subjects were blistered and the fluid applied to other areas on their own skin, as well as to the skin of fresh subjects. The results were entirely negative, and it was concluded that the serum from such blisters had no vesicant action.

The other investigation of this class was a full study of the effects of intravenous injections of dichlorethylsulphide in rabbits, with special reference to

^b Certain autopsy protocols from the laboratory of Hanlon Field are included in Chapter VI.

effects on the blood and the hematopoietic tissues. The results of this work were transmitted in Special Report No. 39, which is included herein. This report describes the tests made in detail. The conditions found in autopsies are recorded and discussed. Charts showing the various body conditions of the animals during the periods of observation, and photographs of internal sections taken in autopsies are also attached. The conclusions define the lethal dose of dichlorethylsulphide when injected intravenously, and the body conditions produced.

LEWISITE I

The much debated question of the effectiveness of Lewisite I as a war gas was studied from the medical standpoint. In general, tests were made in comparison with the effects obtained by a corresponding exposure to mustard gas.

An extensive study of this series is embodied in Special Report No. 38, which described a direct comparative examination of the lesions produced on horses' skin by parallel exposures to dichlorethylsulphide and Lewisite I. This report is included herein. It contains a full study of the histological changes in the lesions produced by dichlorethylsulphide through a period of 32 days from the initial exposure, being the time required for complete reparation of the injured tissues. The comparative study of Lewisite I lesions was not continued longer than the beginning of reparative changes, which was first observed at the end of 48 hours after initial exposure. In addition, the report carries with it photomicrographs of the lesions produced by each substance in various stages of development. The main conclusion from this work was, that necrosis is produced earlier by the Lewisite I, that the reaction is more intense and deeper, but, that reparative changes begin within 48 hours after exposure by Lewisite I. Reparative changes do not begin in the case of mustard gas until the end of the first week after an application of corresponding concentration.

Less extensive tests were made of the effects of Lewisite I on the skin of man. The result of these are noted in weekly reports.¹ The results are not concordant with those obtained on horses' skin. The experiments were carried out with two types of application, namely, as alcoholic solution of equal concentrations, and as the saturated vapors of the two substances. In the first case, single drops of the alcoholic solution being applied to the skin, mustard gas in 0.2 per cent concentration caused erythema but no blister, whereas 1 per cent solution Lewisite I gave no reaction. Five per cent solutions of Lewisite I caused erythema in one case and the formation of a small vesicle in another. However, when 10 per cent solutions were used, the Lewisite I lesion was in the early stages decidedly more severe. The saturated vapors gave nearly equal effects in exposures of seven and one-half minutes. In the actual experiments four out of seven subjects showed the greater reaction to Lewisite I. It should be noted in this connection that the saturated vapor of Lewisite I at 20° contains slightly more than ten times the absolute concentration in milligrams per liter present in the saturated vapor of dichlorethylsulphide at the same temperatures.

The results obtained here on the action of Lewisite I on skin of man, especially those obtained with alcoholic solutions, accord, in general, with the results obtained by the British antigas department, and by the American University Experiment Station. The effects observed when summed up indicate that in minimal concentrations, mustard gas is much more effective in producing lesions. However, beginning with applications of the two substances in amounts per unit of skin area at which Lewisite I first shows effect on human skin, the reaction with Lewisite I increases very rapidly, and with high concentrations considerably exceeds that obtained with dichlorethylsulphide. The reason for this situation may lie in the fact pointed out by the Chemical Warfare Service Laboratory, that Lewisite I is very readily hydrolyzed as compared to dichlorethylsulphide. It may be supposed, accordingly, that small amounts of Lewisite I are hydrolyzed by moisture on the skin surface before penetration, but that Lewisite I, having once actually gained entrance through the skin, produces the more prompt and severe reaction.

A final study on Lewisite I was that of the effects of the intravenous injection into rabbits. Three of these animals were made the subjects of the experiment. One injected with 0.008 gram per kilogram body weight, died immediately. The second, injected with 0.005 gram per kilogram body weight, died three and one-half hours later with massive edema of the lungs. The third injected with 0.001 gram per kilogram showed loss of 100 grams in body weight, but appeared otherwise normal, and survived. This investigation was cut short by the closing of the field.

DIMETHYLTRITHIOCARBONATE

In order to be assured of safety in the use of this substance as a camouflage agent, it was necessary to determine the toxicity of the compound itself out of the presence of mustard gas. The proposed tactical method was described in the Summary Report of the Field Gas and Artillery Sections.² The camouflage material would be employed on fronts where an attack was to be made within a short time. It was accordingly necessary that material to be used should be certainly nontoxic. The results of these tests were communicated in Special Report No. 57, which is included herein. Some reaction on the animals was observed. The tests, however, were severe. They were comprised of such orders of exposure as one-half to two hours in concentrations of 0.73 milligram per liter, and six hours in concentrations of 0.012 milligram, or 1:500,000. If, however, it would be necessary to use only 10 per cent of dimethyltrithiocarbonate in a shell filling to disguise the odor of mustard gas, as the tests described elsewhere have shown, it would not be desirable to use high concentrations in the "fake" mustard gas attacks.

The possible delayed effect of lung lesions followed by secondary infections from exposure to this gas was considered in the work described in Special Report No. 57. However, it appears that the animals upon which tests were made, were taken from a group of which a number were already affected with some form of bronchial trouble or pneumonia. Accordingly, the lesions in the bronchial tubes and lungs found in some of the animals autopsied could not be regarded as evidence of any value on this point. The closing of the field prevented determination of this point.

ROUTINE ANIMAL EXAMINATION

These autopsies were carried out by the Pathological Section for the greater part in connection with field experiments, yet in very considerable number for the chamber experiments on the Physiological Section. The total number of animals examined was roughly between 150 and 200. The examination and results obtained are recorded in every case with the report of the main investigation, of which each formed a part.

MUSTARD-GAS DEFENSE

DETECTION

SNAILS AND OTHER LOW-FORM ORGANISMS

This work was commenced originally to supplement the American University experimentation by testing the possible usefulness of French species of snails for the detection of mustard gas. It was among the earlier studies by the medical sections of the field, and facilities were not available for full laboratory tests. However, the experiments and results recorded in Special Report No. 15 were obtained in response to a telegraphic request from the United States. This report is included herein. It was not found that these French species of snails or slugs could be used as field indicators for mustard gas.

Immediately following the work just considered, the possibility of the use of other species of low-form organisms was taken up. These considered were tadpoles, water insects (*acilius sulcatus*), and mosquito larva. These happen to be forms that were most easily obtained in the immediate vicinity. An experimental field chamber was constructed with capacity of 1 cubic meter. The animals to be tested were placed in a pail of water, and either subjected to a saturated atmosphere of the gas in the chamber, or to a direct addition of blue cross or yellow cross shell filling to the water.

The results of these tests were as follows; (a) Concentrations of 1 c. c. mustard gas to 10 liters of water caused the death of nearly all the forms tested in from 10 to 24 hours, but a pail kept in an atmosphere containing vapor did not affect the animals tested during a period of 24 hours. (b) Concentrations of 1 c. c. blue cross to 10 liters of water produced signs of distress in the animals tested in about half an hour's time, and all died within 12 to 24 hours. When 0.5 c. c. was used in 10 liters of water the same early signs of distress were noted, but there was no subsequent death in the 24-hour period of observation.

It was concluded that these animal forms do not offer sufficiently definite early symptoms in the presence of small yellow cross and blue cross concentrations of shell contents in water to be of much value as "indicators" in the field.

This same general problem was brought forward from time to time again, but no further investigations were made. The possibility of the use, however, of microorganisms as ameba or paramecium were considered. However, because of the difficulties of carrying on proper experimentation at the field, because no data indicated a probable successful outcome of such experiments, and finally, because it was not believed that any microscopic method would be acceptable to officers in the field, such investigations were not reopened.

PHYSIOLOGICAL ESTIMATIONS

In conjunction with the experiments of the chemistry section on the determination of concentrations in mustard gas and air mixtures, physiological tests were studied for the detection and even for the estimation of concentrations of such mixtures. The experiments on the use of sodium platonic iodide as an indicator paper and the animal tests carried out are mentioned in Summary Report of the Chemistry Section.³

A method of different sort was that proposed for the estimation of the composition of shell fillings, by the standardization of the reaction on horses' skin. Alcoholic solutions were utilized, made in dilution in known ratio from the original shell contents. The results obtained showed that the estimation might be made by this method to within 10 to 15 per cent of the concentrations of mustard gas present in the alcoholic solution. These estimations were made on solutions unknown to the observer. However, rather grave discrepancies appear between the estimations of two different observers. This work was not made the subject of a special report, but was noted in a weekly report.⁴

PROTECTIVE EQUIPMENT TESTS

SUITS

A very thorough test was made of the special fabric suit proposed and constructed by the Research Division, Chemical Warfare Service. These tests are embodied in Special Report No. 44, which is included herein. This investigation comprises laboratory tests of the fabric as protection for horses' skin and human skin chamber tests against nominal concentrations and intensive field experiments. The results were in general very favorable to the suit. The protection against mustard-gas vapor, for which the suit was originally designed, was entirely adequate. Further tests with various severe exposures to liquid mustard gas demonstrate that it might not be depended upon too far for such protection. A notable feature of these experiments was the lengths to which the field experiments were carried, and resulted in rather serious effects with some of the subjects.

SAG PASTE

A few comparative tests were made on ointments for protection against mustard gas. These dealt for the most part with preparations already proposed. This work is embodied in Special Report No. 49, included herein. They are, in general, rather unfavorable as to the efficacy of such materials. Among the most important results noted are that these ointments tend rather to delay the development of the lesions than to moderate their ultimate severity, and that while some protection is afforded by sag paste, or hypochlorite ointment, it is rarely complete, and is entirely absent in a considerable portion of cases. It is also noted that horses' skin is not satisfactory for such tests, but that human skin must be used. Sag paste was considered preferable to a mixture of calcium hypochlorite with petrolatum, since it is nonirritating and probably more permanent than the latter.

An experiment was made at Hanlon Field on varying decompositions of protective ointments by the addition of a protein component. It had been reasoned that if dichlorethylsulphide entered into combination directly with

the tissue elements its vesicant powers might be counteracted in this manner. Protein and lipoid fractions prepared from animal tissues were used specifically.

A note on this work was transmitted,⁵ but no greater effectiveness of the ointments was indicated, and the work was not carried further.

TAR FOR HORSES' FEET

The question of finding a material which would protect horses' feet against mustard gas was taken up at separate times in two brief studies. Neither succeeded in determining a satisfactory preparation.

In the first tests tar which had been boiled for three hours to drive off lower fraction was used.

Experiments were made separately to test the protection of the skin of the forefoot and of the frog. The tests on the skin showed that, although immediately after cooling the tar had a smooth hard surface, within a half hour cracks appeared over the tar surface. These extended through the tar covering and exposed the skin underneath. It was seen that such fissures would form traps capable of retaining contaminated earth in contact with the skin. It was concluded that the preparation, on account of its brittleness would be worse than useless if applied for protecting the skin. On the other hand, tests on the hoof itself showed conclusively that no effect or result of lameness could be produced by the most severe exposures to mustard gas, regardless of protection. Accordingly, protection for the frog was unnecessary.

The second investigation was made on material specially prepared for the purpose at the Chemical Warfare Service laboratory. This new preparation was subject to essentially the same defect as the material tried first, though not quite to the same degree. When applied directly, fissures developed some hours later. It was then found that the cracking could be avoided by means of clipping the hair before applying. Yet in face of this latter precaution, in the course of 24 hours the mixture became so softened that it flowed down over the hoof.

The work was carried out and reported shortly before the closing of Hanlon Field.⁶ It is not likely that work would have been taken up again since it had been found, on inquiry of the British, the French, and also the chief veterinarian, A. E. F., that no real need existed for protection of horses' feet against mustard gas.

TREATMENT OF LESIONS

Study of this question was begun very late and actually limited to a test on the effectiveness of potassium permanganate solution in the treatment of mustard-gas burns. The results were conclusively unfavorable. The lesions were obtained by the exposure to the vapor of the purified distillate from German yellow cross shell contained in 4-mm. glass tubes at room temperatures. The tubes contained, at the end opposite from that applied to the skin, cotton moistened with dichlorethylsulphide. The treatment consisted in swabbing with 1 per cent solution of potassium permanganate. In each case four exposures were made, two of which were treated with permanganate solution and two left as controls. In the series of six experiments the treatment was commenced at various periods after exposure and repeated at recorded intervals. It was found that in no case did the treatment alter the course of the mild lesions caused by controlled exposure to mustard-gas vapor.⁷

OBSERVATION OF GAS CASUALTY CASES

A very considerable number of human cases of gas poisoning were studied at certain of the Army hospitals, specifically Evacuation Hospitals No. 1 and No. 2, Base Hospitals No. 15, Nos. 45, and No. 58, and the Justice group of hospitals. Also pathological specimens were received in cases where death occurred. This represented largely deaths from mustard gas and from secondary infection of the respiratory tract. However, except in few cases in the weekly reports, this work was not reported through Hanlon Field, and consequently can not be included here.

SPECIAL REPORT NO. 39. THE EFFECTS OF INTRAVENOUS INJECTIONS OF DICHLORETHYLSULPHIDE IN RABBITS, WITH SPECIAL REFERENCE TO THE BLOOD AND HEMATOPOIETIC TISSUES

INTRODUCTION

1. There exists evidence pointing toward the general toxicity of dichlorethylsulphide, both when administered by inhalation and when injected subcutaneously and intravenously.

(a) Lynch⁸ found that dogs gassed with high concentrations of dichlorethylsulphide—0.3 mgm. per L. for one hour—exhibited symptoms similar to those produced by injection, and not referable to the primary irritation of the respiratory tract. These symptoms were salivation, vomiting, bloody diarrhea, hyperexcitability and convulsions, slow, irregular pulse, becoming rapid before death, and attributed to vagal paralysis. Furthermore, the absorption of dichlorethylsulphide during inhalation was shown by the appearance of the hydrolysis product, dihydroxyethylsulphide, in the urine.

(b) Severe symptoms, ending usually in death within 24 hours, followed the intravenous injection of approximately 0.01 gm. per kilo in dogs. At autopsy, intense congestion, and often extensive hemorrhage into the intestinal mucosa, was the only lesion noted.⁹

(c) Changes in the formed elements of the blood after injection of Yperite have been recorded by Muratet and Fauré-Fremiet,¹⁰ and by Jolly,¹¹ and may be taken as further evidence of the systemic toxicity of this substance.

2. The following report deals with the effects of the intravenous injection of dichlorethylsulphide in rabbits. Special attention was given to the alterations in the blood picture and in the blood-forming organs, since these were the most striking of the results observed to follow the administration of this toxic substance when introduced directly into the blood-stream.

TECHNIQUE

METHOD OF INJECTION

(a) Difficulty was at first experienced in obtaining suitable emulsions for injection. In the earliest experiments the given amount of a 10 per cent alcoholic solution by weight of dichlorethylsulphide was suspended in 0.85 per cent salt solution, shaken vigorously and immediately injected, after allowing the larger globules to settle out. The dose administered was therefore considerably less than the total amount taken. Later it was found that a satisfactory suspension could be made by emulsifying in 30 per cent alcohol in distilled water. A slightly milky emulsion was obtained which, after shaking, did not separate out in the time necessary for injection. The suspension was

prepared from a recently made and accurately weighed 10 per cent solution in absolute alcohol and immediately injected to avoid hydrolysis. The dichloroethylsulphide used was a distillate from a German yellow cross shell content and was actively vesicant.

DOSAGE

No attempt was made to determine accurately the minimal lethal dose. It was found in the earlier experiments that the limit of tolerance was in the neighborhood of 0.01 gm. per kilo body weight, and in the last six rabbits used a uniform dose of 0.005 gm. per kilo was chosen.

SYMPTOMS

1. *Emaciation and loss of weight* was noted in all the rabbits which survived two days or more after the injection. In all but one animal (rabbit No. 12, loss of weight only 100 gms.) this was associated with diarrhea, and perhaps was due to it.

2. *Nervous symptoms*.—These were observed only in rabbits No. 4, No. 9, and No. 13, dying one hour, one and one-half hours, and during the night following the injection. The animals showed extreme restlessness, incoördinate movements, retraction of the head, transient spasticity, but no definite paralyses or convulsions.

3. *Respiratory symptoms*.—No definite or characteristic respiratory symptoms were observed, even in animals dying a few hours after the injection, in which the occurrence of pulmonary embolism might have been suspected.

4. *Diarrhea* occurred in six animals, in all but one associated with the finding of gross lesions of the intestinal tract at autopsy. The feces were copious, fluid dark brown, not grossly admixed with blood or mucus.

5. *Edema of the ears* of wide extent invariably followed injection, even when great care was taken to avoid introducing the material outside the vein. It would appear that the dichlorethylsulphide diffuses readily through the vessel wall. It was also observed that after the injection was begun an area of blanching involving the neighboring skin over a width of several centimeters at once appeared. This persisted for a few minutes after the injection, after which the normal circulation was restored.

PATHOLOGY

RESPIRATORY TRACT

(a) Of 12 rabbits injected, 4 showed definite pulmonary lesions (Nos. 1, 4, 9, 13). These animals all died or were killed within a period of from 1 hour to 22 hours following the injection, and none of the 8 animals surviving over 24 hours has shown significant gross or microscopic lesions.

(b) The changes observed were: (1) Irregular area of edema, in part fibrinous; (2) areas of atelectasis and emphysema; (3) accumulations of leucocytes in the capillaries, often showing caryorrhexis and fragmentation; slight emigration into the alveoli. The trachea and bronchi were normal, except that they contained a homogeneous coagulum. No thrombi were found in the capillaries or larger vessels. The small pulmonary arteries were thick walled and appeared contracted; clear vacuoles were seen beneath the endothelium. The significance of this finding is not clear, as somewhat similar pictures may be seen in normal animals.

(c) It was of course not possible to conclude from the histological findings that dichlorethylsulphide was eliminated by the pulmonary epithelium; on the other hand, no support was found for the view that the lesions were the result of capillary embolism due to impaction of dichlorethylsulphide globules. The fact that animals which survived for a longer period showed no pulmonary lesions might suggest that the edema was the result of a direct and immediate action of the dichlorethylsulphide upon the pulmonary capillaries.

ALIMENTARY TRACT

(a) No lesions were found in the esophagus. Rabbit No. 1 showed hemorrhages into the pyloric portion of the stomach and in the duodenum. Of the remaining rabbits, three (Nos. 20, 24, and 26) had a severe diphtheritic enteritis affecting the middle or lower portion of the small intestine. Rabbit No. 20 showed also patches of membranous inflammation in the large intestine. Rabbit No. 2 also had a diphtheritic colitis, but this proved to be coccidial in origin. Seven rabbits were free from lesions of the intestinal tract.

(b) The liver showed no significant changes.

NERVOUS SYSTEM

(a) No detailed study was made. Capillary thrombosis or hemorrhage were not found.

KIDNEYS

(a) Definite changes were present in the kidneys of only rabbits No. 1 and No. 4. The capsular spaces contained hyaline globules and occasionally red blood cells; hyaline material was also present about the blood vessels in the intermediate zone between cortex and pyramids. Blood cells and hemoglobin (?) casts were found in the collecting tubules. The urine was not examined.

BLOOD AND HEMATOPOIETIC SYSTEM

GENERAL CONSIDERATIONS

The observations of previous workers upon the blood changes following the administration of dichlorethylsulphide having yielded somewhat conflicting results, it was decided to undertake a detailed study of a small series of rabbits, eliminating as far as possible incidental factors which might influence the blood picture. Of these incidental factors, variations in the surrounding temperature were found to be the most disturbing. When rabbits were exposed to a temperature of from 40° to 50° C. for one-half hour, the total leucocyte count showed a tendency to fall, although there were individual exceptions. Counts made shortly after removing the animals from the warm chamber to room temperature (15° to 20°) invariably showed an abrupt and striking rise, as shown in the table and charts (*infra*). After this point had been established, the rabbits during the observational period and following the injection were kept in the laboratory to avoid sudden chilling or abrupt temperature change. Daily counts were made at approximately the same time (9 to 11 a. m.), before food was given. The differential counts are based upon an enumeration of 500 cells, except where the extreme leucopenia made this impracticable. In spite of the usual precautions, unexplained variations occurred which made it

difficult to draw conclusions as to the percental fluctuation. In making the counts, blood was always taken from the uninjected ear. Where both ears had been used, a small cut was made in the skin of the abdomen, and blood taken from one of the superficial abdominal veins. At least two daily counts were made on each rabbit before injection.

ERYTHROCYTES

Stress of other work prevented a detailed study of the numerical variations in the erythrocytes. Preliminary observation (rabbit No. 2) showed no significant change. There were no striking morphological changes pointing to a marked anemia, except perhaps the occurrence of a moderate anisocytosis in the terminal stages. Polychromatophilia was not infrequently seen in smears from normal rabbits. Rabbit No. 27, during the period in which recovery from the effects of an injection was taking place, showed numerous normoblasts—an indication that the erythroblastic tissue had suffered injury, as well as the leucoblastic. Histological study of the bone marrow and spleen afforded further evidence of the toxic action of dichlorethylsulphide upon the formation of red blood cells, which will be described.

LEUCOCYTES

In all but 2 rabbits (Nos. 25, 26) of those surviving more than 24 hours, there occurred after a single injection of 0.005 to 0.01 gm. of dichlorethylsulphide per kilo, a pronounced fall in the number of circulating leucocytes. In these 2 rabbits, a second injection of the same dose after seven days, was followed by the typical reaction. The leucopenia was preceded by a transient rise in only 1 rabbit (No. 24), but it is only fair to state that no counts were made at short periods following the injection. Although degenerated leucocytes with poorly staining and fragmented nuclei and vacuolated cytoplasm were occasionally found in smears, they were infrequent, and even in the presence of an extreme leucopenia the rare leucocytes present in the films were usually normal morphologically. (The data showing the alterations in the blood count are presented in Table 95, and in Charts XXXII to XXXVII.) As regards the behavior of the different types of leucocytes, a study of the data shows the following:

1. In some cases, the injection was followed by an absolute and percental increase in the polymorphonuclears, which fell rapidly with the onset of the leucopenia. In the terminal stages the polymorphonuclears practically disappeared from the peripheral blood.

2. In other cases, an initial fall in the number and percentage of polymorphonuclears was followed by an absolute and relative increase. This secondary rise was associated with the appearance of unripe forms in considerable numbers (rabbits Nos. 25, 27), and coincides with regenerative activity of the bone marrow, as shown by a study of sections from rabbits killed at this stage.

3. The leucopenia was accompanied by a relative lymphocytosis. The absolute number of lymphocytes was diminished in the later stages, and lagged behind the granular cells in cases in which regeneration was occurring.

4. There was a percental increase in the large mononuclear cells, but their absolute number was unchanged or diminished.

BLOOD PLATELETS

Blood platelets were found at all stages, and showed no alterations.

BONE MARROW

1. Although the appearances of the marrow varied in different animals, there was very clear evidence of the destructive effect of the dichlorethylsulphide upon the blood-forming elements. The variations observed could be correlated with varying stages of injury and repair, and these again were reflected more or less closely in the blood picture during life. The following brief descriptions will illustrate the different phases observed.

2. Rabbit 12: Killed four days after injection. At time of death, the leucocyte count had fallen to 400, of which 46 per cent were polymorphonuclears. The marrow of the femur contained a large amount of adipose tissue, the fat cells being separated by a loose edematous tissue containing less than the normal number of cells. The leucocytes of the granulocyte series were almost without exception degenerated. The cytoplasm in sections stained with Wright's stain (normal control) showed no granules. The nuclei stained diffusely and were frequently fragmented. The megacaryocytes also showed degenerative changes. Some of them contained clumps of pink staining, hyaline material in their cytoplasm. There were islands of apparently normal erythroblasts. The blood sinuses were wide and intensely congested with normal-appearing red blood cells; they contained practically no nucleated elements. The appearances were interpreted as indicating an active injury to the bone marrow. The toxic action seems to have affected especially the granular cells.

3. Rabbit 26: Died three days after a second injection of dichlorethylsulphide. Leucocytes on last two days had fallen to 900 and 800, respectively, a smear of the peripheral blood showing very few nucleated cells, and these almost exclusively large and small mononuclears. Sections of the marrow show an extreme aplasia, comparable with that seen in experimental benzol poisoning. Myelocytes, polymorphonuclears, and megacaryocytes have practically disappeared. There are loose collections of normoblasts scattered through the edematous tissue. Occasional globular fragments of chromatin, often inclosed in phagocytes, represent the remains of the destroyed cells. The sinuses are congested and contain no leucocytes. (See fig. 233.)

4. Rabbit 25: Killed on the seventh day following a second injection. The leucocytes, which had fallen to 1,000 on the third day after injection, then rose to 1,400 and 2,100, and at the same time large numbers of myelocytes appeared in the peripheral blood. The histological picture shows the effect of a previous injury and at the same time an active regeneration. The predominant cell type is the myelocyte, the granules of which are definite and well stained in Wright preparations. There is also a fair number of adult polymorphonuclears. The myelocytes are congested in islands, as are also the erythroblasts. Megacaryocytes are numerous and are not degenerated. There are many mitoses. The marrow on the whole is less cellular than normal marrow, and new fat cells are in process of formation. There is much hemosiderin pigment, chiefly intracellular, which may be taken as evidence of previous blood destruction.

5. Rabbit 27: After the first injection, there ensued a fall in the leucocytes from 37,000 to 2,700 on the fourth day, after which there apparently occurred an active regeneration. The count rose again to 32,400, followed by a slight drop to 25,400. At this point a second injection was given, which again was followed by a marked leucopenia, the leucocytes falling to 300 per c. mm., at which point the rabbit was killed. The marrow histologically showed evidence of an initial injury, followed by repair and a fresh destruction of the regenerating cells. There were large areas of almost complete aplasia, similar to that described in rabbit No. 26. But there were also hyperplastic areas, composed of aggregates of large cells with poorly staining nuclei, which under the high power were found to be distorted and obviously degenerating. It would seem that these hyperplastic foci have been again injured by the second injection of the toxic substance.

SPLEEN

1. Changes in the follicles—fragmentation of lymphoid cells with phagocytosis of chromatin particles—were seen in only two of the rabbits (Nos. 1 and 13). (See fig. 234.) Both of these animals died within less than 24 hours after injection. In the remaining rabbits the follicles were normal, or at least showed no signs of either active destruction or excessive proliferation.

2. The sinuses in the majority of the rabbits contained large mononuclear cells laden with blood pigment. The most striking change, however, was the paucity of free cells in the meshes of the reticulum. The sinuses were separated by strands of cells with pale oval nuclei, evidently belonging to the reticular elements.

LYMPHOID TISSUE

1. The two rabbits (Nos. 1 and 13) which showed acute destruction of the lymphoid cells of the splenic follicles also showed cytolysis of the lymphocytes of the thymus and of the intestinal lymphoid tissue.

2. Because of the great susceptibility of the small thymus cells and of the tissue lymphocytes generally to various injurious agents, this was not regarded as a specific effect of the dichlorethylsulphide, particularly as it was not present in those cases in which the destruction of the bone-marrow elements was extreme.

3. In experiments with suspensions of thymus cells *in vitro*, it was found that the permeability of the cells to trypan blue, which may be taken as a sensitive index of injury, was not materially increased by the addition of moderate concentrations of dichlorethylsulphide (less than 1 per cent).

DISCUSSION

1. Of the effects of dichlorethylsulphide when introduced intravenously in rabbits, the most interesting is that upon the blood-forming organs, and upon the leucocyte content of the peripheral venous blood. Within three or four days there may be produced by a single small dose a practically complete exhaustion of the marrow, of granular cells of all types, and a corresponding disappearance of these elements from the blood stream. If the animal survives the initial injection, regeneration occurs and the normal-blood picture is restored. A second injection will cause a renewed injury to the bone marrow.

2. This striking reaction has attracted the attention of other observers. Muratet and Fauré-Fremiet¹⁰ reported upon blood examinations in a series of 6 rabbits, 4 of which were poisoned by inhalation and 2 by subcutaneous injection. In all the animals the following changes were noted: The red blood cells were augmented in number soon after exposure (increase to 6,000,000 to 10,000,000), and then gradually diminished. Nucleated forms were sometimes seen. There was no polychromatophilia or other degenerative change. The leucocytes showed a rise following the intoxicating dose, but later diminished progressively. There was a relative lymphocytosis. Morphologically, degenerative changes were found in the leucocytes. The polymorphonuclears showed abnormal lobulation of the nucleus, dissolution of the granules, and finally a breaking up of the chromatin into spherical masses. The lymphocytes also showed degenerative changes, and many abnormal cells which could not be identified were present in the films.

3. Jolly¹¹ repeated the experiments of Muratet and Fauré-Fremiet¹⁰, using both dogs and rabbits, and administering the dichlorethylsulphide by both inhalation and subcutaneous injection. His results were less consistent than those of the previous workers, but a study of the figures obtained seems to show a rather constant diminution of leucocytes after injection; with inhalation, the results were variable.

4. Zunz¹² observed, in severely gassed human cases, a leucopenia with relative lymphocytosis developing after several days.

5. The similarity of these effects to those produced by benzol bring up the question as to whether it was the dichlorethylsulphide itself, or the chlor-benzene solvent passing over in small amounts into the distillate, or possibly one of the impurities contained in the dichlorethylsulphide, which was responsible for the injury to the hematopoietic tissues. It was hoped to carry out further experiments to determine these points; but it does not seem probable that the very small amount of chlor-benzene which would be contained in the dose of dichlorethylsulphide administered in these experiments would suffice to cause so severe an injury.^c

6. Another interesting feature of the pathology of systemic dichlorethylsulphide poisoning was the frequent occurrence of severe lesions of the intestine. These suggested an elimination of dichlorethylsulphide or its products through the intestinal mucosa, since a direct action after intravenous injection was highly improbable.

7. The significance of the lung lesions has already been discussed. They resembled those caused by gases of the "suffocative" type rather than those produced by inhalation of dichlorethylia. Whether an elimination takes place through the lung was not determined.

CONCLUSIONS

1. The lethal dose of dichlorethylsulphide (distillate from German yellow cross shell) when injected intravenously into rabbits, is from 0.005 to 0.01 gm. per kilo body weight.

2. Rabbits dying within 24 hours showed extensive hemorrhages and edema of the lungs.

3. Severe lesions of the intestinal tract were present in about one-third of the rabbits.

^c Subsequent experiments carried out at the Brady Laboratory, Yale University Medical School, by one of the writers of the report showed that the leucotoxic effect was not due to admixture of chlor-benzene in the shell fillings. (*Journal Experimental Medicine*, 1920, xxxi, No. 1, 71.)

4. Dichlorethylsulphide, injected intravenously, is specifically poisonous for the hematopoietic tissues. Severe lesions were caused in the bone marrow and the number of circulating leucocytes was markedly diminished. In animals surviving the injection, regeneration occurred. The granular cells of the bone marrow seem to be more sensitive than the lymphoid cells and the erythrocytes.

PROTOCOLS ^a

RABBIT 1 (serial No. 6).—Healthy animal; weight, 2,030 grams before exposure. August 30, 1918, at 12.30 p.m. received intravenous injection of dichlorethylsulphide in marginal vein of ear.

Dose.—One-hundredth cubic centimeter of pure dichlorethylsulphide, or 0.005 c. c. per kilo of body weight, in the form of a 10 per cent alcoholic solution freshly prepared, 1 c. c. of which was added to 4 c. c. of normal saline.

August 20, 4.45 p. m., seemed very weak and apathetic; 7 p. m., still very weak; ears and body very cold; developed a profuse watery diarrhea. August 21, 10.20 a. m., still very weak but seems much better. Killed by a blow on the back of the neck. Autopsy at 11 a. m.

Gross findings.—*Respiratory tract:* Injection of submucous venules of trachea. *Lungs* show some interstitial and irregular dark red areas scattered through all lobes. *Gastrointestinal tract:* Fresh submucous hemorrhages in the pyloric end of the stomach. For a distance of 5 to 6 cm. below the pyloric end, the duodenal wall shows numerous fresh hemorrhages. The rest of the intestinal tract is normal. Other organs normal.

Microscopic findings.—*Trachea* is normal. *Lungs:* Section shows irregular congestion of alveolar wall with an increased number of polymorphonuclear leucocytes in capillaries and alveolar lumen. In the congested areas the alveoli are partially collapsed. The nuclei of the leucocytes show marked pyknosis and fragmentation. There are patchy areas of edema, sometimes with a little fibrin. In other places there are hemorrhages into the alveolar lumen. In one slide, there is a distinct area of bronchopneumonia; a vessel at the apex of this area contains a fresh thrombus. The *bronchi* are generally normal except that they often contain red blood cells and coagulated edema fluid. *Stomach:* There are several small areas of focal hemorrhagic necrosis with beginning leucocytic reaction. *Duodenum:* The glandular tubules are separated in many places by fresh hemorrhages. The leucocytes in the extravasated blood are pyknotic and fragmented. The surface epithelium in places is necrotic. *Spleen:* The follicles are largely replaced by large reticular cells with pale nuclei and indefinite cell outlines. The small lymphocytes at the margin of the follicles are pyknotic and fragmented. Large phagocytes filled with chromatin fragments are found in pulp and lying in sinuses. *Thymus:* Cytolysis of the small thymus cells; nuclear fragments inclosed in phagocytes. Epithelial components of gland unchanged. *Kidney:* Globular coagulum in the capsular spaces. Changes not very marked.

RABBIT 2 (serial No. 15).—Young healthy animal. Weight before exposure, 2,125 grams. August 20, 1918, at 12 m., received intravenous injection of dichlorethylsulphide in marginal vein of ear.

Dose.—Five one-hundredths cubic centimeter, or 0.025 c. c. per kilo of body weight, in the form of a freshly prepared 10 per cent alcoholic solution diluted with normal saline.

Injection produced no immediate effect. Rabbit showed progressive emaciation. Died August 25, at 11 a. m. Autopsy 15 minutes after death. Body weight, 1,760 grams.

Gross findings.—Emaciation. Moderate pulmonary emphysema. *Gastrointestinal tract:* Diphtheritic colitis of large intestine. *Spleen:* Flat and soft.

Microscopic findings.—*Lungs:* Emphysema present, with some fresh alveolar hemorrhage. *Spleen:* Follicles normal. The red blood cells are practically in pulp reticulum; none in sinuses. Sinuses contain large multinuclear cells with abundant cytoplasm, which contain much brown pigment.

RABBIT 4 (serial No. 10).—Healthy animal. Weight before exposure, 2,025 grams. August 22, 1918, at 3.20 p. m., received intravenous injection of dichlorethylsulphide in marginal vein of ear.

^aThe charts include only those animals in which blood counts were made during a preliminary observational period.

Dose.—Five one-thousandths cubic centimeter per kilo of body weight, given in a 10 per cent alcoholic solution diluted with normal salt solution.

At 4.30 p. m., rabbit was found in convulsions, showing opisthotonos, spastic paralysis of hind legs, with occasional clonic spasms, rapid dyspnea, etc.; 5.20 p. m., died.

Gross findings.—Organs appear normal aside from hemorrhagic areas in the lungs.

Microscopic findings.—*Lungs:* Patchy areas of edema and irregular congestion. There is no true bronchopneumonic process present. *Spleen:* Normal follicles; no cytolysis of lymphoid cells. Sinuses not congested, nor do they contain abnormal elements. Other organs are not markedly abnormal.

RABBIT 9 (serial No. 41).—Healthy female. Weight before exposure, 2,120 grams. August 30, 1918, received intravenous injection of dichlorethylsulphide in marginal vein of ear.

Dose.—Five one-thousandths cubic centimeter per kilo of body weight, given in a freshly prepared 10 per cent alcoholic solution diluted with saline.

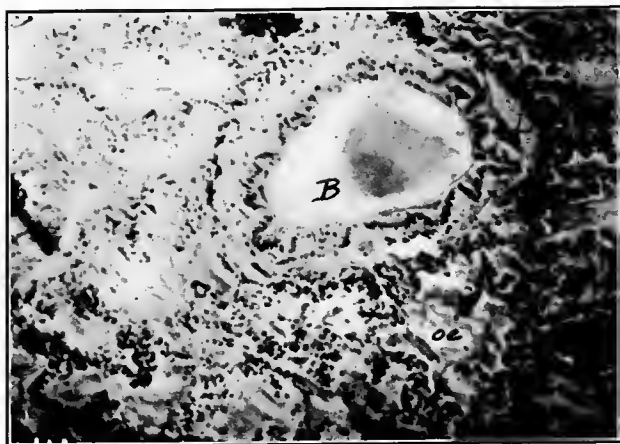


FIG. 229.—Rabbit 9, serial No. 41. Death $2\frac{1}{2}$ hours after second injection of dichlorethylsulphide. Lung: Edema (α) in part fibrinous. Stasis of leucocytes (Le) in capillaries. Coagulum in bronchus (B) and distension of peribronchial lymphatic vessel (L)

pycnotic and caryorrhectic. Bronchial epithelium is normal; submucous edema and leucocytic infiltration is present in some of the bronchi. (Fig. 229.)

RABBIT 12 (serial No. 97).—Healthy half-grown female. Weight before exposure 1,620 grams. September 16, 1918, at 2.30 p. m., received intravenous injection of dichlorethylsulphide in marginal vein of ear.

Dose.—One-hundredth cubic centimeter of dichlorethylsulphide per kilo of body weight in the form of a 1 per cent solution in 30 per cent alcohol and distilled water freshly prepared. Progressive emaciation and weakness until death. September 20, 1918, at 3 p. m., killed by blow on back of the neck. Autopsy September 20, at 3.15 p. m. Weight at autopsy 1,520 grams.

Gross findings.—Normal. *Intestinal tract* normal. Rest of the organs are practically normal.

Microscopic findings.—*Lungs and gastrointestinal tract,* normal. *Spleen:* Follicles normal. Atrophy of the pulp tissue. Large spindle-shaped cells occur in the walls of the sinuses. *Bone marrow:* Fat cells are present in some numbers, and the fatty tissue shows edema. The marrow is much depleted of its cells. There are no normal polynuclears and no granulated myelocytes. The cytoplasm of the megacaryocytes shows some degenerative changes. Mitoses are rare. Fragmentation of cells is fairly common. There are numerous nucleated red blood cells. The vessels are congested and contain many nucleated cells.

RABBIT 13 (serial No. 55).—Healthy female; half-grown; weight before exposure, 1,660 grams. September 16, 1918, at 2.30 p. m., received 0.016 c. c. of dichlorethylsulphide, or 0.01 c. c. per kilo of body weight. This was given as a 1 per cent solution in 30 per cent alcohol and distilled water freshly prepared. Rabbit was accidentally choked while being

No symptoms followed this injection. September 2, 1918, 10 a. m., injection repeated; 11.30 a. m., animal began to show convulsive movements, with periods of rest during which she lays on her side; diarrhea; 2 p. m., killed.

Gross findings.—Frothy discharge from nose and mouth; frothy fluid in esophagus and trachea. Lungs show areas which are sunken and dark red in color. Other organs normal.

Microscopic findings.—*Lungs:* Patchy areas of edema, some part of coagulum being definitely fibrinous. The capillaries are congested and crowded with leucocytes. The nuclei of these are very often

injected, but she speedily recovered. Later, convulsive movements developed, which were incoordinate rather than paralytic. Died, September 17, early in morning. Autopsy, September 17, at 8.15 a. m. Weight after death, 1,550 grams.

Gross findings.—*Lungs* appear to be edematous. Other organs are normal.

Microscopic findings.—*Lungs*: Patchy edema; irregular areas of congestion where the alveoli are partially collapsed. Many polynuclear leucocytes in capillaries or even in the alveolar lumen. The bronchi contain a small amount of edematous fluid but are otherwise normal. *Spleen*: In pulp, scattered cells show fragmentation, caryorrhexis and some pigment containing cells. Follicles show extreme destruction of lymphoid cells. Active phagocytosis in center of follicle of the fragmented cells by large mononuclear cells with abundant cytoplasm. *Thymus*: Destruction of lymphoid cells in the center of the lobule and phagocytosis by large mononuclear cells. (Fig. 230.)

RABBIT 20 (serial No. 96).—Healthy female rabbit. Weight before exposure, 1,850 grams. September 16, 1918, at 2.30 p. m., received intravenous injection of dichlorethylsulphide in marginal vein of ear.



FIG. 230.—Rabbit 13, serial No. 55. Died in less than 18 hours after intravenous injection of dichlorethylsulphide, 0.01 g. per kilo. Spleen, showing caryorrhexis of cells of follicles, with phagocytosis of chromatin fragments



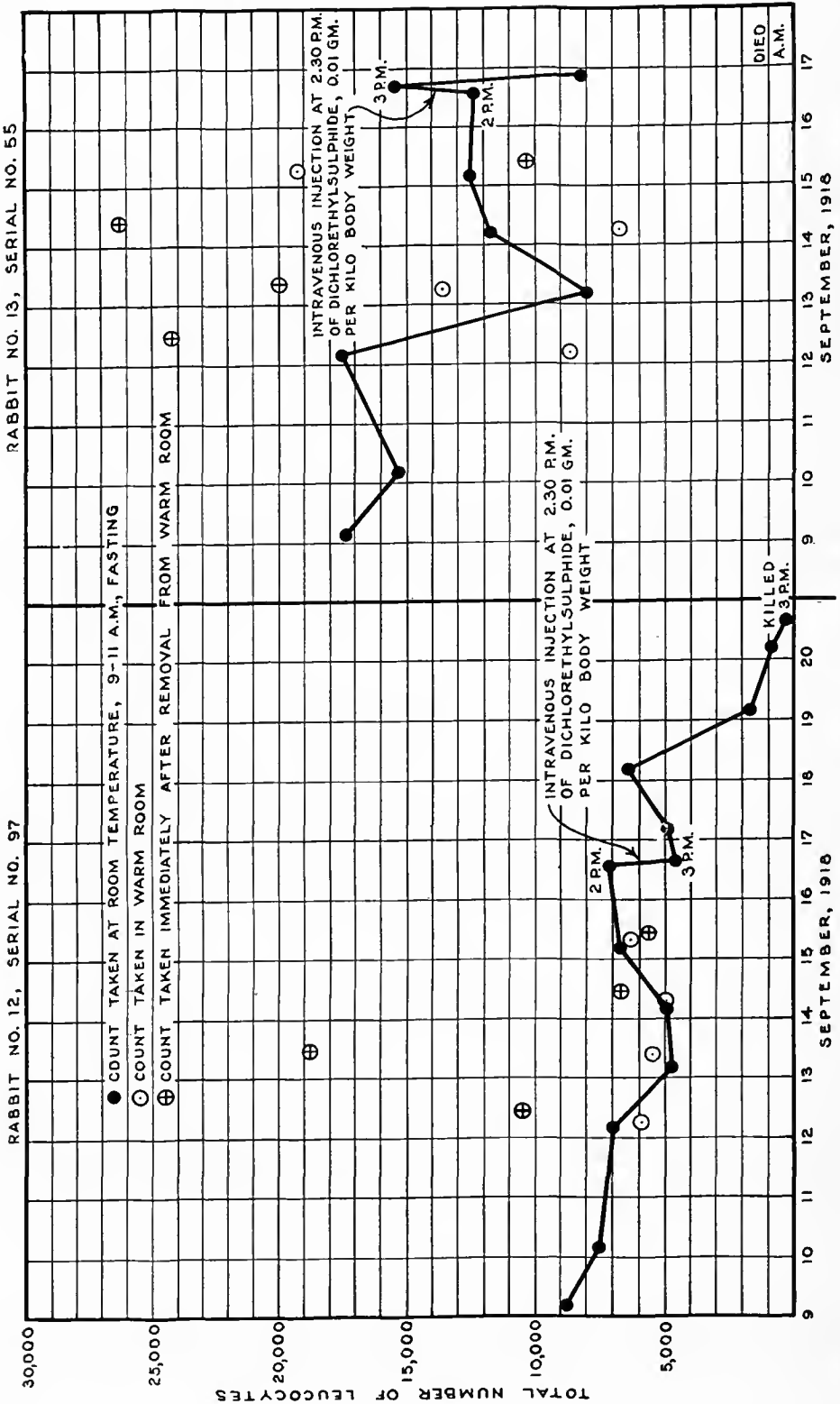
FIG. 231.—Rabbit 20, serial No. 96. Died 4 days after injection of 0.1 gm. per kilo intravenously. Small intestine: Complete hemorrhagic necrosis of mucosa (M); extreme fibrinous edema of submucosa (Oe)

Dose.—One-hundredth cubic centimeter of dichlorethylsulphide per kilo of body weight in the form of a 1 per cent solution in 30 per cent alcohol and distilled water freshly prepared. Lost weight steadily from date of injection. Weight September 19, 1,550 grams. Diarrhea, very profuse, noticed on September 19. This persisted until death. Died, September 20, at 10 a. m.

Autopsy.—Weight before autopsy, 1,485 grams.

Gross findings.—*Lungs* normal. *Gastrointestinal tract* normal. The lower 30 cm. of the small intestine and patchy areas in the cecum are the seat of a necrotic enteritis. Other organs are normal.

Microscopic findings.—*Lungs* are normal. *Small intestine*: Partial to complete necrosis of intestinal epithelium. Numerous thromboses in capillaries of submucous layer. Intense submucous edema. *Spleen*: Follicles are composed of normal cells showing no fragmentation. Pulp contains very few cells and shows swollen reticula. Sinuses contain many large mononuclear cells with brown pigment in cytoplasm. *Bone marrow*: Shows many adult fat cells between which are numerous islands of myelocytes, polynuclear leucocytes, and nucleated red blood cells. The blood sinuses are congested, but contain very few nucleated cells. In the marrow, the number of megacaryocytes is normal. A few mitotic figures can be seen; some of the cells are fragmented, but there is no phagocytosis or pigment formation. The marrow presents evidence that it has suffered recent injury with early regeneration. (Fig. 231.)



RABBIT 23 (serial No. 141).—Healthy adult female. Weight before exposure, 2,000 grams. September 23, 1918, at 10 a. m., received intravenous injection of dichlorethylsulphide in marginal vein of ear.

Dose.—Five one-thousandths cubic centimeter per kilo of body weight, given in a 1 per cent solution in distilled water and 30 per cent alcohol freshly prepared. Progressive weakness and emaciation from day of injection. September 26, weight 1,900 grams. Diarrhea on September 27. Died, September 28 at 6 a. m. Autopsy. September 28, at 8.15 a. m. Body weight at death, 1,813 grams.

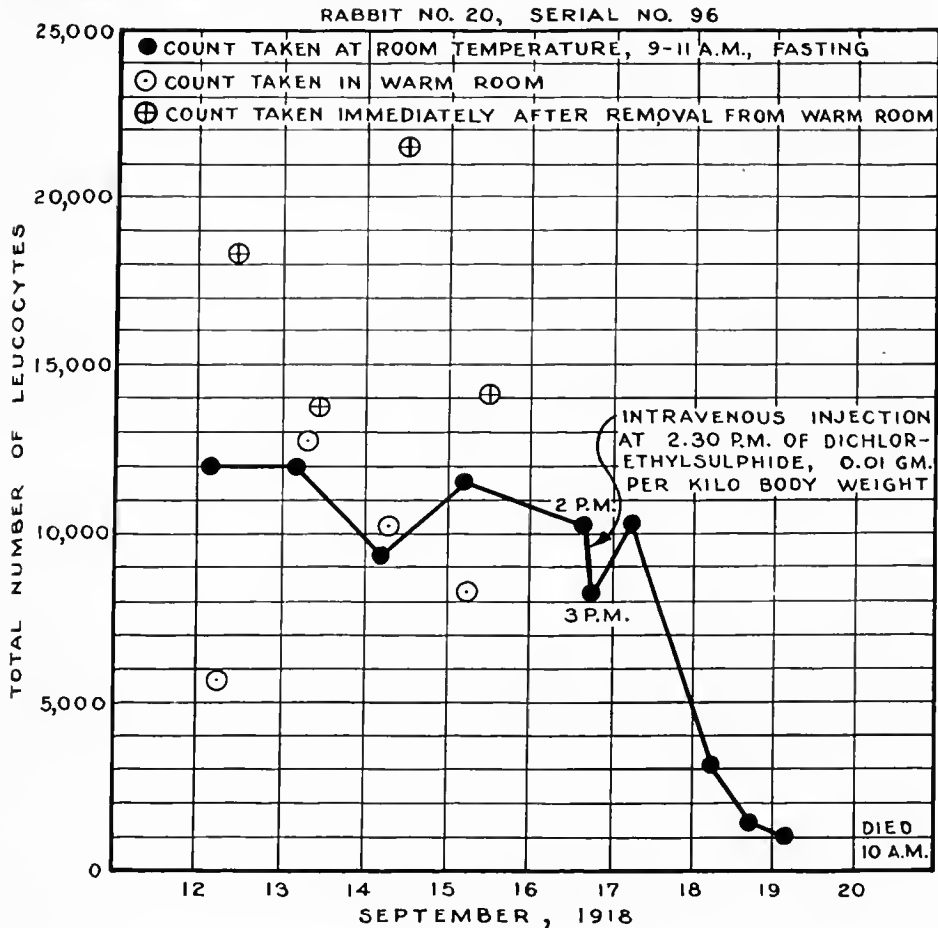


CHART XXXIII

Gross findings.—Lungs: Normal. Intestinal tract presents no lesion, but the small intestine is full of an abundant mucoid secretion, while the large intestine is full of mushy unformed fecal material of a brownish color.

Microscopic findings.—Spleen: There are no changes in the follicles. The sinuses are distended and there are many large mononuclear cells containing pigment. Bone marrow: There are not many fat cells present. Polynuclear leucocytes, myelocytes, and megacaryocytes, however, are very abundant. (Fig. 232.) There are not many nucleated red blood cells. There are a few mitoses; some fragmentation can be seen.

RABBIT 24 (serial No. 104).—Healthy rabbit. Weight before exposure, 1,770 grams. September 23, 1918, at 10 a. m., received 0.005 c. c. of dichlorethylsulphide per kilo of body weight as an intravenous injection in the marginal vein of the ear. It was given in a 1 per cent solution in 30 per cent alcohol and distilled water freshly prepared. Progressive weakness and moderate emaciation up to day of death. September 26, weight, 1,715 grams. Diarrhea just before death. September 27, at 7.30 a. m., died. Autopsy at 8.15 a. m., September 27.

Gross findings.—*Lungs:* Normal. *Gastrointestinal tract:* Middle two-fourths of small intestine seat of a necrotic enteritis. Contents are a thin and watery mucus. The wall of the large intestine is normal, but the contents consist of much abundant mushy fecal material. No formed feces present.

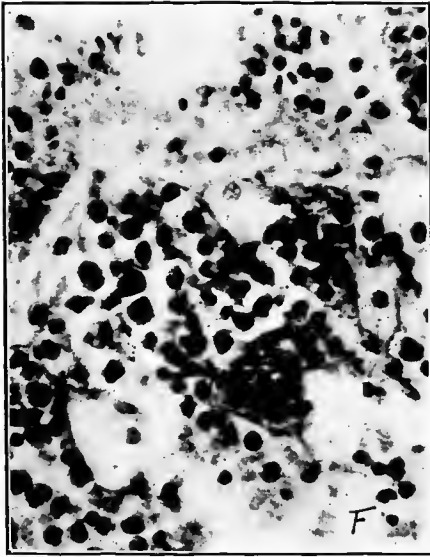


FIG. 232.—Normal rabbit. Bone marrow of femur. Megacaryocyte (M)

shows some degenerative changes. There is, however, no fragmentation, phagocytosis, edema or pigment formation. (Fig. 233.)

RABBIT 25 (serial No. 168).—Healthy rabbit. Weight before exposure, 1,800 grams. September 23, 1918, at 11 a. m., received intravenous injection of dichlorethylsulphide in marginal vein of ear.

Dose.—Five one-thousandths cubic centimeter per kilo of body weight in a 1 per cent solution in distilled water and 30 per cent alcohol, freshly prepared. No symptoms followed this injection. Weight, September 26, 1,800 grams. October 1, injection repeated at 11 a. m. Progressive loss of weight followed. October 4, weight 1,580 grams. October 7, at 4 p. m. killed by a blow on back of head. Autopsy at time of death. Weight at death, 1,450 grams.

Gross findings.—Organs are apparently normal.

Microscopic findings.—*Lungs:* Slight emphysema and areas of patchy congestion. *Spleen:* Follicles are normal. Many large pigment cells in the sinuses. Very few wandering cells in sinuses. *Bone marrow:* Numerous embryonic fat cells, numerous islands of myelocytes, nucleated red cells and megacaryocytes, and numerous mitoses, present. There are not many polynuclear leucocytes. Pigment cells, however, are numerous. The marrow is actively regenerating.

Microscopic findings.—*Intestine:* A necrotic membrane covers a submucous layer from which the epithelium has been desquamated. The underlying tissues are congested and infiltrated with various inflammatory cells. The epithelium which remains in the comparatively healthy areas is normal. Clumps of bacteria are present on the mucous surface. The centers of the Peyer's patches show a few areas of cellular destruction and caryorrhexis. *Spleen:* There is no destruction of cells in the follicles. Some of the follicles show areas which are entirely composed of epithelioid cells. The sinuses are distended with red cells, among which are large phagocytes filled with pigment. Between the sinuses are only cells of the reticular type. *Bone marrow:* The marrow is composed of many fat cells, numerous polynuclear leucocytes, granular myelocytes and islands of nucleated red cells. The cytoplasm of the megacaryocytes

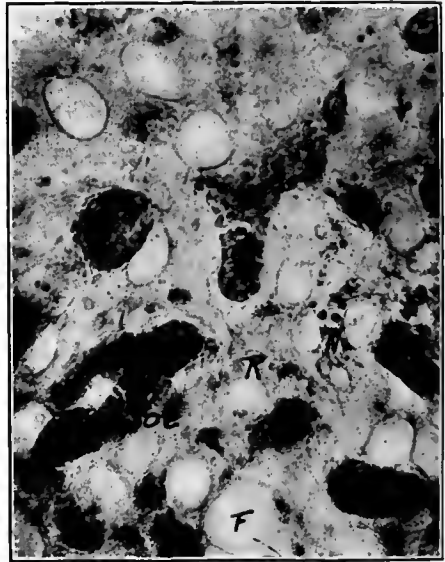


FIG. 233.—Rabbit 24, serial No. 104. Died 3 days after second injection of dichlorethylsulphide, 0.005 gm. per kilo intravenously. Bone marrow of femur, showing extreme aplasia. The sinuses (B) are wide and congested. In the edematous pulp (oe) are many fat cells (F). Myelocytes, polymorphonuclears, and megacaryocytes are absent. There are few islands of normoblasts (N). The pale nuclei (R) are those of the reticular cells. (Somewhat lower magnification than Figure 232.)

RABBIT 26 (serial No. 174).—Healthy adult male. Weight before exposure, 2,045 grams. October 1, 1918, at 11 a. m., received intravenous injection of dichlorethylsulphide in the marginal vein of the ear.

Dose.—Five one-thousandths cubic centimeter per kilo of body weight given in 1 per cent solution in distilled water and 30 per cent alcohol freshly prepared. No symptoms followed first injection. October 7, at 11 a. m., injection repeated. Body weight, 2,050 grams. Progressive emaciation followed, with weakness. Profuse diarrhea occurred on October 10. Died, October 11, at approximately 6 a. m. Autopsy, October 11, at 8.30 a. m. Body weight at death, 1,860 grams.

Gross findings.—*Gastrointestinal tract:* Stomach normal. *Small intestine:* Lower 25 cm. of ileum is the seat of a necrotic enteritis. Large intestine is filled with fluid fecal material. The wall is normal. Other organs are normal in the gross.

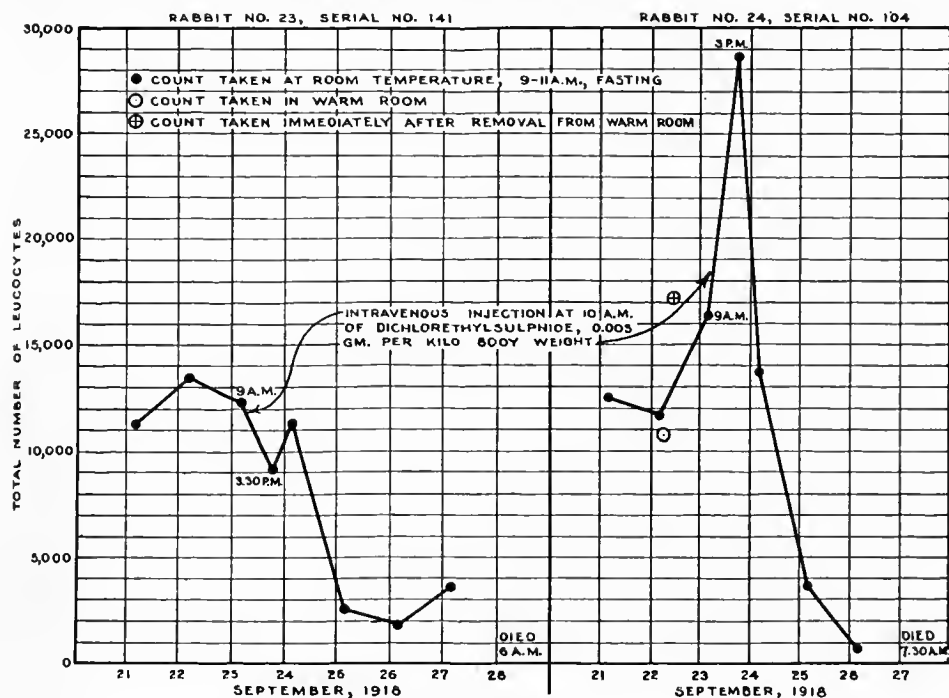


CHART XXXIV

Microscopic findings.—*Small intestine:* Necrotic pseudomembrane, polynuclear infiltration of submucous layer, and congestion of blood vessels. Desquamation of intestinal cells occur in some areas. *Spleen:* The pulp is depleted of cells, the follicles are atrophic. There are numerous large pigment cells in the sinuses. *Bone marrow:* Embryonic fat cells are present throughout the entire marrow. The marrow is entirely depleted of cells, except for a few islands of normoblasts. A few cells are fragmented, and occasionally some phagocytosis is seen. Myelocytes, polynuclear leucocytes, and megacaryocytes are generally absent. The marrow has been subjected to a marked destructive change.

RABBIT 27 (serial No. 177).—Healthy adult female. Body weight before exposure, 1,680 grams. October 1, 1918, at 11 a. m., received intravenous injection of dichlorethylsulphide in the marginal vein of the ear.

Dose.—Five one-thousandths cubic centimeter per kilo of body weight given in 1 per cent solution in distilled water and alcohol freshly prepared.

After this injection the animal became somewhat weaker. Body weight October 7, 1,628 grams. Gradual recovery. October 7, at 11 a. m., the injection was repeated. Animal again became much weaker and somewhat emaciated. October 10, weight 1,605 grams. October 11, at 11 a. m., killed by blow on head. Autopsy at time of death.

Gross findings.—*Bone marrow* rather grayish in color. Other organs normal.

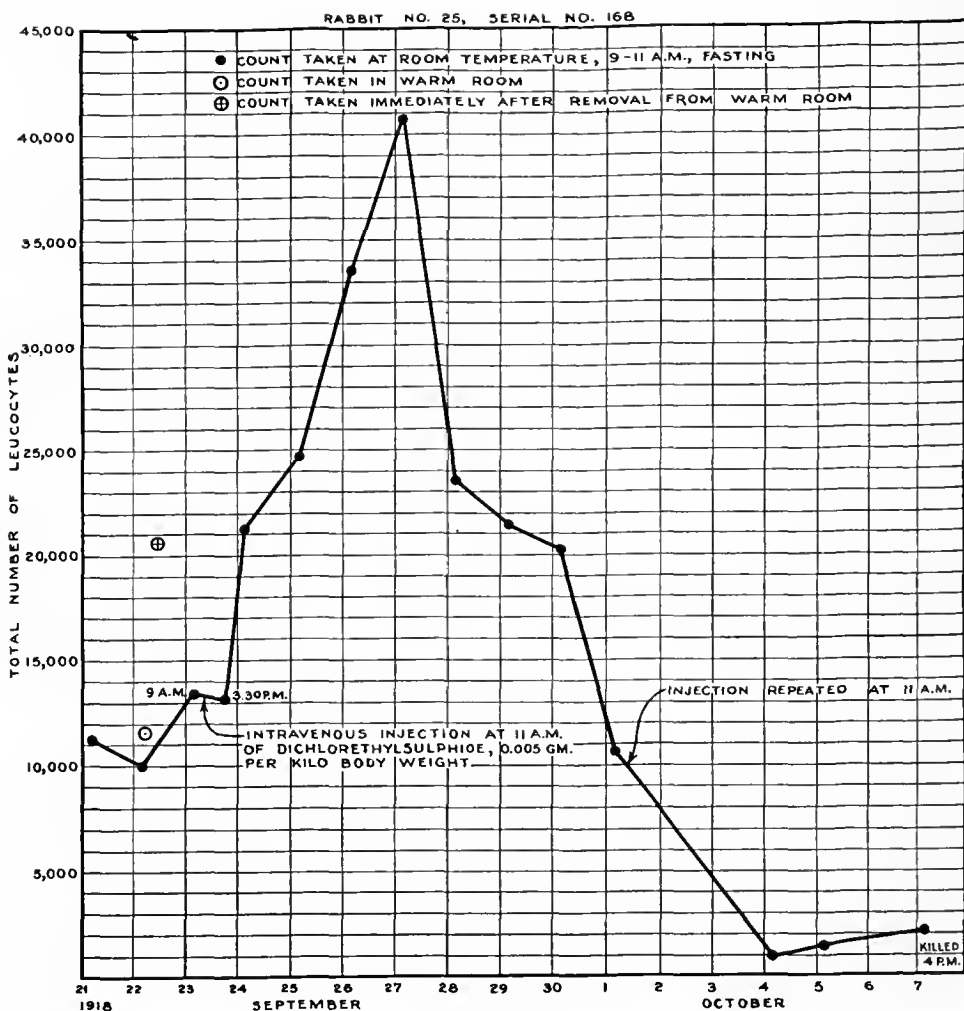


CHART XXXV

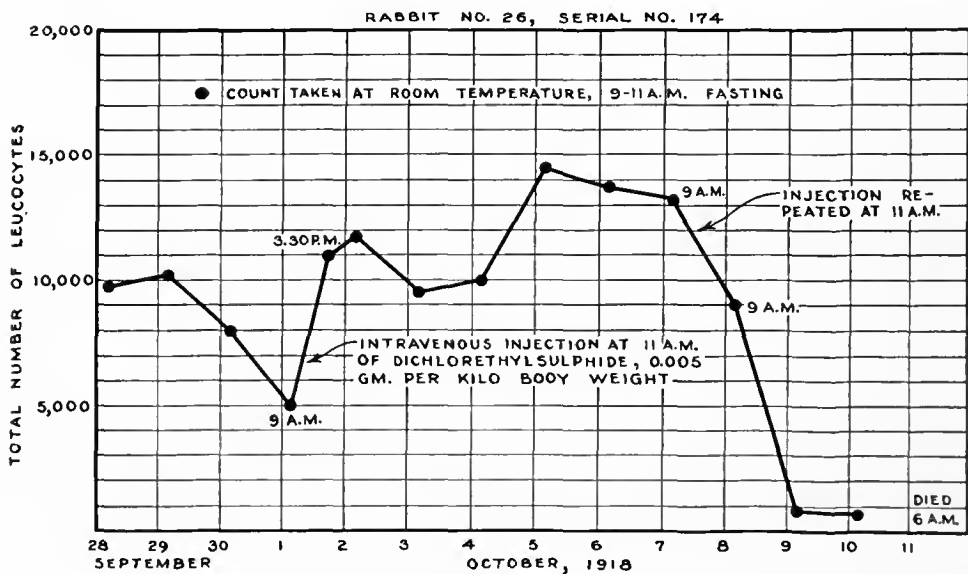
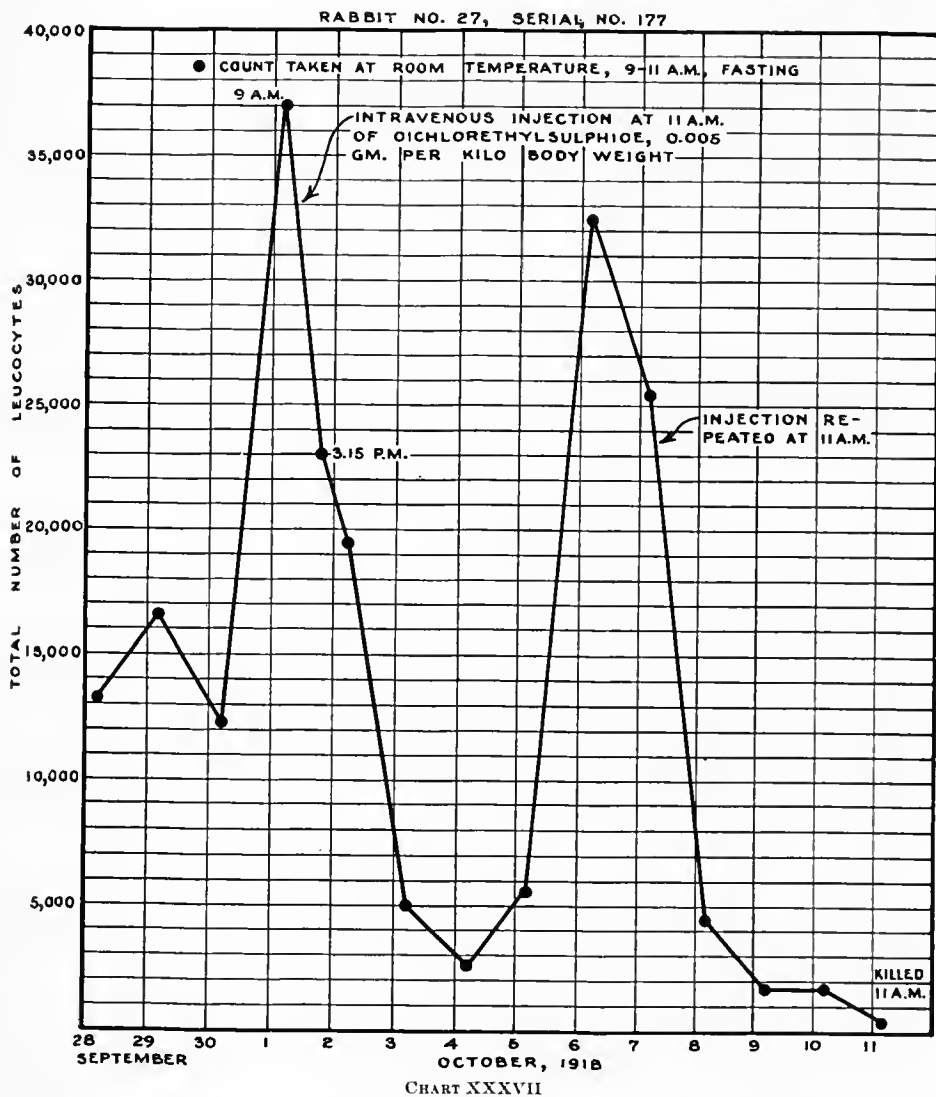


CHART XXXVI

Microscopic findings.—*Spleen:* Follicles are normal. Pulp contains very few wandering cells. The sinuses are crowded with huge mononuclear cells with abundant cytoplasm which contain loads of brown pigment. *Bone marrow:* Part of the bone marrow is depleted of all marrow cells and the fatty tissue is edematous. In another area which is hyperplastic there



are quite a few cells present, including many abnormally lobulated leucocytes, and a few islands of nucleated red blood cells. Scarcely any of the normal bone marrow cells are present. There are a few megacaryocytes and some pigment-containing cells. The peculiar picture is probably due to the toxic action of the second injection on a marrow which is actively regenerating.

[illegible]

Myelocytes (?), 43 per cent.

SPECIAL REPORT NO. 38. THE CUTANEOUS LESIONS CAUSED BY DICHLOR-ETHYLSULPHIDE AND LEWISITE IN THE HORSE ***LESIONS CAUSED BY DICHLORETHYLSULPHIDE****TECHNIQUE**

(1) Recently prepared 10 per cent alcoholic solutions of the distilled contents of a Yellow Cross German shell, were applied to the shaved skin of horses over areas of 7 mm. in diameter, 0.1 c. c. being introduced into a glass tube held against the skin and allowed to evaporate. A few lesions resulting from other concentrations and methods of application were studied, but, in general, this procedure was followed in order to obtain comparable lesions at different intervals. When cocaine was used for excision the skin was infiltrated in a circle at a distance from the affected areas. The pieces taken included a segment of adjacent normal skin.

(2) The tissue was fixed in Zenker's fluid, embedded in paraffin, and stained with hematoxylin-eosin, Van Gieson, Gram-Weigert, and by Weigert's method for elastic fibers. Considerable difficulty was experienced in obtaining satisfactory sections of the late stages, the dried necrotic tissue being extremely hard to impregnate and section.

GROSS APPEARANCES

(1) A few hours after exposure there develops a soft edema slightly more extensive than the area of application. The extent of the edema varies with the site of application, being greater in the loose tissue over the shoulders than upon the back or rump. On the following day the swelling has begun to subside, and soon disappears completely. The exposed skin then hardly differs perceptibly from the adjacent normal skin, except in being slightly smoother, more glistening, and, in certain cases, is a shade darker. Mayer¹³ has well described the hardness which is perceptible to palpation as conveying the sensation of a disk or plaque of cardboard inclosed in the skin. This superficial induration persists. After a week or 10 days, a scaly desquamation is observed at the margin of the indurated area, which in the course of the next week becomes sharply defined. The central plaque, composed of dead mummified tissue, becomes sequestered from the underlying tissue, at first at the margin, eventually over the entire area, until it is finally cast off completely. There is active growth of new hair beneath the slough and one has the impression that the edges are actually pushed up by the growing hairs. The new hairs are usually lighter in color.

(2) After the casting off of the slough, it is discovered that complete healing has taken place beneath the dead tissue. The area is covered with a smooth, glistening epidermis devoid of pigment; and the area remains practically pigment free for at least two months, and perhaps permanently.

(3) Tenderness becomes marked on the second day and seems to last for a long while. Palpation causes a twitching of the skin muscles and evident distress.

* Although an excellent and detailed study of the lesions caused by the application of mustard gas and other vesicant substances to the horses' skin has been carried out by Mayer (report, *Extrait du Procès verbal de la séance du Février, 1913*), it seems desirable to report briefly upon a similar study conducted at Haddon Field.

HISTOLOGICAL CHANGES

(1) *Piece excised one hour after exposure.*—(a) The epidermis, sweat and sebaceous glands, hair follicles are normal. (b) Corium normal. Blood vessels moderately filled with normal appearing blood cells. Very few wandering cells in the subepidermal connective tissue. Mast cells are fairly numerous about the blood vessels. (c) The only noticeable lesion is a slight edema in the form of a granular coagulum, especially noticeable about the roots of the hair follicles. The edema is somewhat more marked in the subcutaneous connective tissues, where the collagen fibrils are separated by granular coagulated material. Capillaries and lymphatics are not distended; there is no accumulation of leucocytes. No changes are noted in the endothelial cells

(2) *Pieces excised six hours after exposure.*—The appearances are identical with those seen after one hour, with the following exceptions; (a) The edema is considerably more marked, especially in the subcutaneous tissue. (b) There is a rather marked distension of the lymphatics, which contain a granular coagulum identical with that between the collagen fibrils. There are occasional eosinophiles, mast cells, and mononuclears in the vicinity of the vessels, but no definite inflammatory reaction of a cellular nature.

(3) *Pieces excised 11 hours after exposure.*—(a) Over the area of maximal edema, in the section, the epidermis is stretched and the papillary folds obliterated. In general there are no abnormal appearances in the superficial epithelial cells, nor in those belonging to the epidermal appendages. A few follicles, however, are definitely injured. The earliest recognized

alteration is a hydropic change in the epithelial sheaths. Later, there is leucocytic infiltration and destruction of the shaft of the hair. The epithelial cell nuclei become shrunken and pycnotic. The corium in the affected area is somewhat looser in texture than the normal corium and is obviously slightly edematous. The capillaries are moderately filled with red blood cells. There is no excess in the number of leucocytes. The edema of the subcutaneous tissue is well marked, perhaps slightly more intense than in the six-hour specimen. (Fig. 234.) The small vessels show a moderate marginal accumulation of polymorphonuclear leucocytes, with slight emigration into the adjoining cellular tissue. Eosinophiles are quite numerous. A few distended lymphatic vessels are present in the depth of the section.



FIG. 234.—Dichlorethylsulphide, 11 hours after exposure. Collagen fibers (C) separated by granular coagulum (oe). Distended lymphatic vessel (L). Emigrated leucocytes (le)

(4) *Piece excised 24 hours after exposure.*—(a) The findings do not differ materially from those in the 11-hour section. The edema continues to be marked; there is no increased leucocytic reaction. In fact this feature is less striking than in the 11-hour section. No edema is noted in the corium.

(5) *Piece excised 48 hours after exposure.*—(a) The edema and distension of the corium has led to the flattening of the overlying epidermis, with partial obliteration of the normal folds. The hair follicles and glands appear less concentrated in the affected area than in the normal skin. The epidermis, itself, is much thinned over the area of the lesion. The pigment is concentrated to such a degree that the finer changes in the cells are obscured. It is possible, however, to make out definite signs of injury to the epidermal cells. This is shown in two ways: A diffuse, intense staining of the nucleus, with loss of chromatin structure, and moderate shrinkage; or there may develop in the cytoplasm an unstained vacuole, which, as it increases in size, causes a concentric compression of the nucleus, and finally leads to its disappearance. In this way the cell comes to contain an unstained, oval clear space surrounded by dense pigment clumps. The early stages of this process, which picks out individual cells, can best be traced at the margin of the lesion or in the less densely pigmented cells of the hair follicles.

(b) It is impossible at this stage of the lesion to distinguish sharply between the living and the dead portions of the epidermis. No clear line of demarcation has been established.

(c) In all the sections examined there appear small areas in which the epidermis is completely destroyed and replaced by a dense collection of leucocytes, the nuclei of which are much fragmented. Pigment granules and the debris of the destroyed cells enter into the formation of these superficial pustules. They may or may not be covered by a thin layer of pigment-containing keratin cells. They appear to originate in the corium, since one may find dense localized accumulations of leucocytes, without destruction or extensive invasion of the overlying epidermis. Usually the pustules are situated adjacent to a hair follicle. One shows a distinct vesicle with a gelatinous thready material, separated from the corium by a dense marginal zone of leucocytes.

(d) Very interesting changes are found in the epidermal appendages. There is partial necrosis of the hair follicles in the affected area. This obviously proceeds from within outwards, the hair shaft and the inner sheath cells often showing marked degenerative changes while the more external cells are still well preserved. So, also, there is in many of the sebaceous glands a well-circumscribed area of necrosis, which regularly affects that portion of the gland which abuts upon the hair shaft, leaving the peripheral cells unaltered. The degenerating sebaceous cells stand out sharply by reason of their brightly red-stained cytoplasm, and the marked shrinkage and subsequent fragmentation of their nuclei.

(e) The sweat glands show less severe changes than the sebaceous glands. Certain acini, however, show necrosis of individual cells with caryorrhectic changes in the nuclei and hydropic swelling of the protoplasm of the cells.

(f) The corium is less edematous than in the earlier stages of the lesion. Here and there can be seen a slight separation of the collagen fibrils, and occasionally a fine fibrinous network can be found under the high power. Distended lymphatic channels containing a pink coagulum can be found in the

deeper layers of the corium. A definite injury to the connective tissue is evident only in the superficial zone immediately underlying the epidermis. Here the nuclei of the connective tissue cells are degenerated, the collagen fibers fused and hyaline, and the elastic fibrils fragmented. Throughout the corium, there is a loose infiltration of leucocytes, chiefly polymorphonuclears. The denser focal accumulations at certain points immediately beneath and within the epidermis have been described. As the emigrated cells approach the surface, their nuclei undergo caryorrhexis.

(g) The capillaries of the corium are well filled with red blood cells. Only a few of the smallest vessels in the papillary layer show fusion and homogenization of the cells suggesting hyaline thrombi. Most of the capillaries even in this zone are quite normal. No definite alterations are found in the endothelial cells.

(6) *Pieces excised 72 hours after exposure.*—(a) Over the affected area, the epidermis is thinned to about one-third the normal width. Measurements of the normal area show an average width of 17.2 as compared with an average width of 6.2 in the area of the lesion.^f

(b) In the normal skin three zones can readily be distinguished, namely: 1. The stratum corneum, consisting of only one or two layers of flat, platelike cells. 2. The stratum granulosum, four to five cell layers deep. 3. The stratum mucosum, composed of one or two layers of cells, with distinct oval nuclei ranged with long axis at right angles to the surface. The distribution of pigment in the normal skin is somewhat irregular, but is in general as follows: While the cells of the stratum mucosum invariably contain abundant pigment, oftenest in the form of a granular crescentic cap at the superficial pole of the nucleus, the pigment is much less abundant in the middle zone. In the flattened horny cells there is often a good deal of pigment in the form of coarser clumps.

(c) The pigment in the affected skin area shows striking differences from this normal distribution. Whether there is an actual increase in the amount of pigment is rather difficult to say. The cells are more closely aggregated and appear compressed, probably by the pressure of the swollen tissue underneath. There is thus undoubtedly a concentration of pigment granules. On the other hand, the pigment granules are clumped into larger masses than the normal granules. The large branching chromatophores in the subjacent tissue are more numerous than beneath the normal area.

(d) The nuclei of the epithelial cells in the thinned-out layer covering the exposed area refuse the stain and have probably lost their structure. Their original outline, however, is still evident from the distribution of the pigment about them.

(e) The epidermis rests upon a wavy structureless pink-staining band, which is not evident in the normal skin.

(f) Immediately beneath this, is a zone of dense cellular infiltration. In it one may distinguish the nuclei of still intact polymorphonuclear leucocytes, but the nuclear material is for the most part fragmented and distorted into wisps and clumps of bizarre shape.

(g) The skin appendages show marked lesions. The sheaths of epidermal cells surrounding the hair follicles are in various stages of disintegration or in

^fThese numbers refer to divisions on the micrometer eyepieces.

some instances, completely necrotic, and invaded by leucocytes. The sweat glands are also severely damaged, the glandular epithelial cells appearing hydropic, ragged, undergoing caryolysis, and finally disintegrating completely. The sebaceous glands seem to be somewhat more resistant; but individual cells and even entire glands are found showing degenerative changes.

(h) The connective tissue of the corium is severely injured. In the more superficial portions, the nuclei have wholly disappeared; the outlines of the collagen bundles are no longer distinct, the fibers fusing into a homogeneous pink-staining material, loosely invaded by polymorphonuclear leucocytes. Deeper down, the connective tissue is not necrotic; the connective tissue nuclei and the collagen fibrils stain normally; there is, however, considerable edema.

The lymph vessels show moderate distension.

(i) Capillaries filled with normal-appearing red blood cells can be traced up to the papillary layer of the corium and appear to be lined with normal endothelium. Whether the small terminal loops are thrombosed can not be made out clearly because of the dense cellular infiltration; there is no evidence of thrombosis or other vascular injury in the deeper tissues.

(7) *Piece removed at autopsy 98 hours after exposure.*—(a) The section includes very little normal skin. As the area of the lesion is approached there are numerous small pustular foci, some wholly within the epidermis itself, others immediately beneath it or in-



FIG. 235.—Dichlorethylsulphide, 98 hours after exposure. Superficial pustules (p) at margin of lesion. Increased pigmentation (pg) in adjacent epithelium. Leucocytic infiltration of corium

volving only the basal portion of the epidermis. (Fig. 235.) These pustules are apparently free from bacteria (Gram-Weigert-safranine). Over the entire area of the lesion the epidermis is thinned and the nuclei stained diffusely and indistinctly. There is again an apparent increase or concentration of pigment.

(b) The superficial zone of corium is very densely infiltrated with leucocytes, although these are separated from the overlying epidermis in most places by a narrow hyaline zone which is free from cells. (Fig. 236.) The nuclei of the leucocytes show extreme caryorrhexis, and are often drawn out into the most irregular shapes, like molten lead. In this mass of broken up nuclear material the connective tissue cells can not be distinguished.

(c) The edema of the deeper portions of the connective tissue is not marked. Degenerative changes in the follicles, sebaceous and sudoriparous glands are evident throughout the section, although individual structures vary in degree to which they are affected. There is a scattered infiltration of polymorphonuclear leucocytes throughout the depths of the corium, with dense localized accumulations about some of the follicles and glands.

(d) The immunity of the blood vessels is again quite striking. Even in some of maximal leucocytic infiltration, capillaries containing normal red-blood cells and showing no distinct lesions, are found.

(e) Reparative changes are not yet present, nor has definite sequestration of the injured tissue begun.

(8) *Piece excised seven days after exposure.*—(a) Epidermis: Proceeding from the healthy margin, the epithelium as it approaches the area of exposure becomes thinned out, and at the junction, which is rather abrupt, there is a partial exfoliation of the superficial layers. Proceeding toward the center, the epidermis becomes elevated from the underlying corium by an accumulation of leucocytes, mixed with fibrin and cell detritus, immediately beneath it. The leucocytes at the base of the pustule are still preserved; near the surface they are much fragmented and distorted. This area probably corresponds to the indurated ridge which can be felt at this stage in the living animal at the margin of the affected area.

(b) Over the summit of the leucocytic accumulation the epidermis is extremely thin, and in places difficult to recognize as a continuous layer, being obscured by the mass of nuclear debris. In general, however, the alignment of the epidermal cells is preserved, even when the nuclear staining is lost.

(c) Proceeding centrally beyond the limits of this pustular ridge, the epithelium is found to be preserved as a thin continuous layer, in which the nuclei are represented by unstained oval spaces, surrounded by pigment. The pigment clumps are coarser and apparently more abundant than in the normal epithelium at the margin. From the basal layer of the healthy epithelium at the edge of the lesion there may be traced under the pustular area and for some distance beyond a tongue of epithelial cells. (Fig. 237.) These form a continuous sheet of irregularly flattened cells with large pale nuclei and fibrillated cytoplasm. They contain little or no pigment. They are continuous with the cells of the hair follicle sheath lying at the same depth, which also are characterized by very large pale nuclei. There appears to be, indeed, a very active growth of new epithelium about the base of these follicles. Mitoses are quite frequent, and the cells not only have hypertrophic atypical nuclei,



FIG. 236.—Dichlorethylsulphide, 98 hours after exposure. Thinning of epithelium (E), infiltration of corium (c) with leucocytes showing caryorrhexis. Degenerate follicles (II)

but they do not show the orderly alignment and progressive keratinization of the inner layers seen in the normal follicles. Similar changes are noted in the follicles which underlie the central portion of the lesion.

(d) The intense leucocytic infiltration and consequent destruction of the corium at the edge of the lesion has been described. Farther centrally the epidermis rests upon a layer of dense but apparently necrotic tissue in which there is also toward the surface a dense collection of material showing caryorrhexis. The nuclear masses which are derived from invading leucocytes lie beneath a somewhat swollen membrana propria. There is very little infiltration into the cells of the epidermis itself. The necrosis of the superficial zone of the corium is evidenced by the partial fusion of the collagen fibrils into a uniform pink-staining material and by the loss of the connective tissue nuclei.



FIG. 237.—Dichlorethylsulphide, seven days after exposure. Beginnings equestration of necrotic epithelium (E₁) and superficial corium (C) by ingrowth of regenerating epithelium (E₂). Proliferation of cells of sheaths of hair follicles (H₁, H₂)

epidermis; the blood vessels and their contents in the deeper portions of the corium are quite unaltered, even in places where the skin appendages show the effects of the injury.

(h) The *elastic fibers* in the zone of superficial injury have largely disappeared, only faintly staining fragments persisting. About the regenerating hair follicles, the very characteristic arrangement of the elastic fibers, in the form of parallel bands, joined at the epithelial margin by vertical stays, is no longer recognizable.

(9) *Piece excised 14 days after exposure.*—(a) The appearances do not differ materially from those in the one week's specimen. Regenerative changes are somewhat more advanced. *Epidermis:* Over the neighboring healthy

(e) In this zone of superficial necrosis all the normal skin structures are more or less completely disintegrated. The *hair follicles* are surrounded by epidermal cells, the nuclei of which are distorted and pyknotic. Often they are invaded by leucocytes, which in turn have become fragmented. The *sebaceous glands* also show degeneration of the nuclei of the gland cells and are often the seat of dense leucocytic invasion.

(f) The small *nerves*, so far as can be judged in hematoxylin-eosin and Van Gieson preparations, are severely injured. This is shown by swelling of the endoneurium and perineurium, and by degenerative changes in the sheath nuclei.

(g) The small *capillaries* in the necrotic zone are filled with a brownish staining material which, as the healthy tissue beneath is approached, can be seen to be derived from fused and altered red blood cells. This change is limited to the superficial zone immediately beneath the necrotic

region, there is perhaps a somewhat increased pigmentation. This ceases abruptly as the lesion is approached, and for a short distance near the margin the epidermis is virtually pigment-free. There is also in this region slight hyperkeratosis. (Fig. 238.) The tongue-like continuation of the epidermis can now be traced for a considerable distance beneath the superficial sequestering dead epidermis. (Fig. 239.) In places, in a study of a number of sections, small islands of flattened epidermal cells which appear to take their origin about partially degenerated hair follicles are found, and seem to be independent of the growing epithelial processes arising at the margin of the lesion. Individual cells of the new-forming epidermis are highly atypical. Hypertrophic cells with nuclei three or four times the normal volume are common. (Fig. 240.)

(b) The original layer of dead, thinned, and deeply pigmented epidermis is still present, attached to a layer of necrotic corium, filled with distorted chromatin masses derived from invading leucocytes and from the degenerated fixed elements of the necrosed tissue. There are many large branching chromatophores. The blood vessels are filled with brown material derived from altered red corpuscles, but their outlines are still preserved.

(c) The demarcation of the dead tissue from the underlying living corium is very sharp and distinct; in many places it is marked by a zone of leucocytic infiltration. In this transitional zone, the collagen fibers are swollen and hyaline. Between them, the connective-tissue cells have taken on the character of fibroblasts, the nuclei becoming large and vesicular. Isolated mononuclear and polymorphonuclear leucocytes are scattered amongst the connective-tissue fibers.

(d) The blood vessels in places still contain an excess of polynuclears and are frequently surrounded by small cells. There are occasional collections of eosinophiles.

(e) About many of the necrotic hair follicles, there is occurring an active proliferation of epithelial cells, frequently showing mitosis, and often very atypical in size and staining. Regenerative changes are not very evident in the sudoriparous glands, although the secreting cells occasionally show alterations, irregularity of arrangement, darker staining of cytoplasm, hypertrophy of the nuclei of individual cells, which suggest a more active growth. No mitoses were found. There is, however, an active proliferation of fibroblasts about groups of glands, frequently with collections of eosinophiles and scattered lymphoid cells.



FIG. 238.—Dichlorethylsulphide, 14 days after exposure. The sequestration of the dead epidermis (E) and the underlying necrotic tissue (C) by ingrowth of regenerating epithelium (E₂). Desquamated keratin (K)

(10) *Piece excised 32 days after exposure* (obtained at autopsy).—(a) The block includes a loose, button-shaped cap of necrotic issue, 2 to 3 mm. thick which is already detached from the underlying living tissue. Because of the difficulty of impregnating and sectioning this dried, crumbly, material, its microscopic structure could not be studied.

(b) The original site of application is completely covered with new-formed epithelium. This differs from the healthy epithelium at the margin in being distinctly thicker; roughly, from two to three times the average width of the contiguous epidermis. The alignment of the cells is irregular. Pigment formation is beginning, but the amount formed is insignificant. The new-formed epidermis sends very irregular processes into the corium, whereas in the normal epidermis, the basal boundary forms an even line. The hair follicles are completely regenerated throughout the affected area and do not differ obviously from the normal follicles. The sweat and sebaceous glands likewise show no evidence of previous injury. The superficial layer of corium differs from the normal in its looser texture and in the slightly irregular arrangement of the collagen fibrils, which in the normal corium tend to run parallel to the surface. There are still occasional wandering cells present.

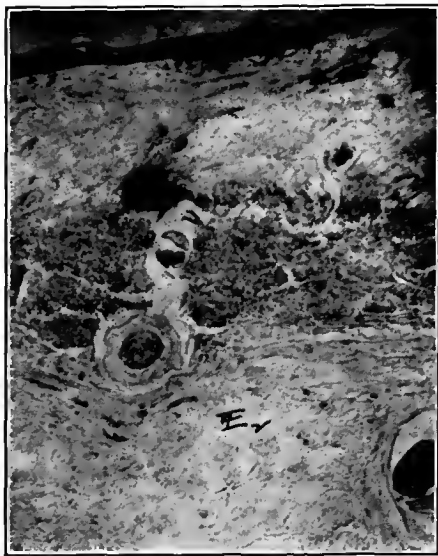


FIG. 239.—Dichlorethylsulphide, 14 days after exposure. Same designations as Figure 238

DISCUSSION

The history of the dichlorethylsulphide lesion, therefore, is somewhat as follows:

(1) The primary visible evidence of injury is an edema affecting the deeper layers of the corium, appearing early, and gradually subsiding. The reabsorption is accompanied by disten-

tion of the lymphatic vessels. The exudate is for the most part non-fibrinous.

(2) The necrosis of the epidermis takes place very gradually by a process of mummification, in which there is no dislocation of the individual cells. Even after several weeks the basal cells are not disintegrated and their original nuclei are still recognizable as oval clear spaces. There occurs a clumping and concentration of pigment, and possibly during the earliest stages, an increased pigment production.

(3) The necrosis of the epidermis and of the superficial portion of the corium does not appear to depend upon a primary vascular thrombosis. In the early phases of the process, capillaries with intact red blood cells and endothelium are found to extend almost to the surface epithelium. Later they share the fate of the superficial tissues, the blood cells fusing into a brownish

mass, and the nuclei of the endothelial cells shrinking and becoming pycnotic. The deeper vessels, aside from the changes incidental to the inflammatory reaction, show no evidence of injury.

(4) The alterations in the nuclei of the emigrated leucocytes and also of the fixed connective tissue cells in the zone of the injury are very striking.

(5) The penetration of the toxic agent along the shafts of the hair follicles is rendered probable from the fact that the injury to these structures and to the sebaceous glands evidently proceeds from within outwards.

(6) Reparative processes begin toward the end of the first week by an intrusion of a flat tongue of regenerating epithelium between the superficial zone of necrosis and the underlying healthy tissue. The sheaths of the hair follicles play an active rôle in the regeneration, the cells proliferating and establishing connections with the epithelial processes growing in from the healthy margin. The new epidermis is at first pigment-free and contains many atypical cells. The preservation of the basal portion of many of the hair follicles explains the renewed growth of hair beneath the dead sequestrum.

LESIONS CAUSED BY LEWISITE

TECHNIQUE

(1) Twenty-five one-hundredths cubic centimeter of a 10 per cent alcoholic solution were applied over areas of shaved skin measuring approximately 0.05 sq. cm. For comparison, the same amount of a 10 per cent alcoholic solution of dichlorethylsulphide was applied to a neighboring area. Pieces were excised for histological study after 5 hours, 24 hours, and 48 hours. No study has been made of the late lesions.



FIG. 240.—Dichlorethylsulphide, 11 days after exposure. Hypertrophic cells at margin of hair follicles

GROSS APPEARANCES

(1) After five hours the lesion caused by Lewisite involved approximately three times the area of the lesion caused by dichlorethylsulphide and was also more elevated. During excision it was observed that the Lewisite lesions occupied roughly three times the area of the mustard-gas burn; the tenderness and induration were more marked, and the pigmentation distinctly deeper. The same differences in intensity were noted after 48 hours, but subsequently became less marked.

HISTOLOGICAL CHANGES

(1) *Piece excised five hours after application of Lewisite.*—(a) The epidermis is distinctly thinned. There is increased pigment, especially at the margin of the lesion, and in certain hair follicles. No degenerative changes in the epi-

dermal cells, but some of the epithelial cells of the hair follicles show beginning vacuole formation. The most striking feature is a very marked edema of the cutis and as much of the underlying connective tissue as is included in the section. There is wide separation of the connective-tissue fibers and of the epidermal appendages by a granular coagulum. The more superficial capillaries are crowded with normal appearing red blood cells and contain no excess of leucocytes. There is no obvious injury to the endothelium. The deeper vessels, both the small arterioles and the capillaries, show marked changes. They contain red blood cells of altered staining reaction, and are surrounded by loose collections of polymorphonuclear leucocytes. The nuclei of the emigrated cells are pycnotic and hazy. No dilated lymphatics are found in the sections.

(2) *Piece excised five hours after application of dichlorethylsulphide.*—(a) There are no marked changes in the epidermal cells of the skin or hair follicles.



FIG. 241.—Lewisite No. 1, 24 hours after exposure. Edema leucocytes in corium (L), congestion of superficial capillaries (B) early degenerative changes and thinning of epidermis (E)

Occasional cells show the presence of an unstained vacuole, with compression of the nucleus. There is very moderate edema of the corium. There is no marked congestion. About a few of the capillaries are loose aggregations of wandering cells, amongst them many eosinophiles. There are no lesions of the sweat glands or sebaceous glands.

(3) *Piece excised 24 hours after application of Lewisite* (fig. 241).—*Epi-*

dermis: Thinned over lesions, with loss of papillary folds. Alteration of staining in certain areas, increased affinity for eosin. Shrinkage and diffuse staining of nuclei. Vacuolar degeneration of nuclei of individual cells at margin of lesion.

(b) *Corium:* Papillary edema, with foamy, clear spaces immediately beneath epidermis. Leucocytic infiltration, quite dense in places, in all layers of corium and in subcutaneous tissue. The predominant cells are polymorphonuclears, eosinophiles are scarce. There is not the extreme fragmentation of nuclei seen in dichlorethylsulphide preparations. (c) *Appendages:* Hair follicles, same changes as in epidermis. Sweat glands, individual acini show complete necrosis with pycnosis, fragmentation, and eventual complete disappearance of nuclei. (d) *Blood vessels:* Marked congestion throughout. Platelet thrombi in some of the vessels. No marked distention of lymphatics.

(4) *Piece excised 24 hours after application of dichlorethylsulphide.*—(a) *Epidermis:* Vacuolar degeneration of individual cells. Slight flattening. No change in staining reaction. Similar findings in cells of hair follicles. Sweat and sebaceous glands show no lesions. (b) *Corium.* Moderate edema. Loose and scattered infiltration of wandering cells. Many eosinophiles. (c) *Blood vessels:* Normal. No marked congestion.

(5) *Piece excised 48 hours after application of Lewisite* (fig. 242).—(a) *Epidermis*: At the edge of the lesion, there is a very abrupt transition between the living epidermis and the dead epidermis. The latter is thinned and stains diffusely and intensely with eosin. Only the nuclear outlines persist, but all chromatin staining is lost. The healthy epithelium has already begun to push its way for a short distance beneath the dead epidermis. There is the same apparent increase in the density of pigment that was noted in the mustard lesions. (b) *Epidermal appendages*: In the affected area, the epithelial cells surrounding the hair follicles stain diffusely with eosin. The nuclei are shrunken and diffusely stained. The sebaceous glands are similarly affected. (c) *Corium*: The superficial portion is moderately edematous; the outlines of the collagen fibrils are indistinct. There is a sparsity of nuclei, and such nuclei as are still present show pycnosis. Leucocytic infiltration is present only at the margin; over the summit of the lesion the corium is practically free of wandering cells. The deeper layers of the corium, on the other hand, are diffusely invaded with leucocytes. These do not show the caryorrhexis which is so striking in the mustard-gas lesions. (d) *The subcutaneous tissue* is very edematous, the fibers being separated by a fibrinous exudate. The vessels are filled with leucocytes and the perivascular sheaths are infiltrated with them. A number of the large veins contain thrombi.

No histological study of the reparative stages of the Lewisite lesions has been made.

SUMMARY

A comparison of the earlier changes brought about by the two substances in equal concentration shows the following histological differences: 1. Lewisite produces an earlier necrosis of the epidermis. 2. The edema produced by Lewisite is more extensive than that caused by mustard gas, and the exudate is definitely fibrinous. 3. The Lewisite does not so definitely penetrate along the shafts of the hair follicles. 4. The inflammatory reaction appears sooner with Lewisite than with mustard gas and is more intense and deeper. The emigrated leucocytes do not undergo early caryorrhexis. 5. Vascular thrombosis is a more conspicuous feature with Lewisite than with mustard gas. 6. Beginning reparative changes in the epithelium were observed after 48 hours in the case of the Lewisite lesion; they did not begin until the end of the first week after application of corresponding concentration of mustard gas.



FIG. 242.—Lewisite No. 1, 48 hours after exposure. Transition between living epidermis (E₁) and dead epidermis (E₂). Leucocytic infiltration at margin of lesion (Lc), edema of deeper layers (oe)

SPECIAL REPORT NO. 57. TOXICITY OF DIMETHYLTRITHIOCARBONATE

The sample of dimethyltrithiocarbonate used for the following tests was a pure specimen, free from dimethylsulphate, furnished by the gas service laboratories.

The concentrations in the test chamber were obtained either by heating the liquid on an electric hot plate or by spraying an alcoholic solution. The atmosphere within the chamber was kept constantly in motion by means of an electric fan. The temperature in the chamber during exposure was about 15° C. The figures for concentration in the table below are nominal: no successful analyses of the air within the chamber were carried out. The boiling point of dimethyltrithiocarbonate is said to be almost exactly the same as that of dichlorethylsulphide and it has been assumed that the vapor pressures of the two substances at various temperatures are of the same order. If experience obtained with dichlorethylsulphide applies to dimethyltrithiocarbonate, one should expect actual concentrations to be about one-third the nominal.

The only animals available were rabbits, guinea pigs, and white mice. The stock of guinea pigs and mice appeared to be quite sound; the stock of rabbits was not so sound as could have been wished; at the time of the experiments, many showed slight nasal discharge and a few died showing signs of bronchopneumonia. The surviving animals were killed with hydrocyanic acid in from two to six days after being exposed. In experiments W-6 to W-10, inclusive, approximately half the total number of animals surviving were killed in two days and the remainder at the end of four days.

TABLE 96.—*Effect of dimethyltrithiocarbonate upon animals*

Ex- peri- ment No.	Concentra- tion (parts of air con- taining 1 part sub- stance)	Con- centra- tion (milli- grams per liter)	Dura- tion of expo- sure (hours)	How vaporized	Number of animals						Survivals killed	Observations
					Rab- bits		Guinea pigs		Mice			
					Died	Gassed	Died	Gassed	Died	Gassed		
W-5	1-2,850	2.19	2	Heat.....	2	2	0	4	1	4	6 days...	1 rabbit died 3 days; 1 in 4 days; 1 mouse in 2 days.
W-2	1-8,550	.73	1	do.....	0	2	0	4	0	4	5 days...	1 mouse died 1 day.
W-1	1-8,550	.73		do.....	0	2	0	4	1	4	5 days...	
W-10	1-8,550	.73	1	Spraying..	0	3	0	3			(2 days...	1 rabbit died 1 day.
W-3	1-8,550	.73	2	Heat.....	0	2	0	4	0	4	5 days...	
W-4	1-8,550	.73	2	Spraying..	0	2	0	4	0	4	5 days...	
W-9	1-8,550	.73	2	do.....	1	3	0	3	0	3	(2 days...	
W-7	1-100,000	.062	16	do.....	0	3	0	3	0	3	4 days...	
W-6	1-500,000	.0123	16	do.....	1	2	0	3	0	3	4 days...	
W-8	1-1,000,000	.006	18	do.....	0	3	0	3	1	3	4 days...	1 rabbit died 3 days. 1 mouse died 1 day.

¹ Chamber cleared and a fresh concentration raised every two hours.

SYMPTOMS DURING AND AFTER GASSING

In the experiment (W-5) in which a concentration of 1 to 2,850 was used, the symptoms exhibited by the rabbits were: Sneezing and salivation, together with some listlessness and gasping movements which persisted for some time. After two days both of the rabbits had a thick nasal discharge. There was a loss of appetite. The guinea pigs showed lacrymation and sneezing in the chamber, but behaved normally thereafter. The mice breathed deeply while exposed, but on removal from the chamber, although lively, seemed to hold their eyes closed. Later one mouse was found moribund and died.

With lower concentrations the animals might become excited, sneeze, rub their noses, become quiet, and seemed depressed, but appeared perfectly normal after removal from the gassing chamber.

CONCLUSIONS

On the basis of the results, tabulated above, it may be concluded that dimethyltrithiocarbonate is a substance of low toxicity. In view of the pathological findings, given below in detail, further conclusions can not be drawn at this time.

Autopsies and histological examinations of the lungs and trachea of 25 rabbits, 35 guinea pigs, and 26 mice used in physiological experiment W are summarized in tabular form as follows:

TABLE 97.—*Pathological report*

No. of experiment	Serial No.	Animal	Lesions	L/BW	L/H	L/K	Grade of casualty
W-1	329	Rb	Negative	0.005	1.89	0.78	N.
W-1	330	Rb	Slight bronchitis; anemia; emaciation	.005	2.1	.65	C.
W-1	331	GP	Scattered areas of bronchopneumonia	.009	3.0		B.
W-1	332	GP	Moderate edema; hemorrhages	.011	3.0		B.
W-1	333	GP	Hemorrhages				C.
W-1	334	GP	Slight edema; hemorrhages	.011	2.43		C.
W-1	336	Mo	Patchy edema				B.
W-1	337	Mo	do				B.
W-2	338	Mo	No histological examination				(?)
W-2	335	Rb	Normal	.004	1.5	.65	N.
W-2	339	Rb	do	.005	1.6	.69	N.
W-2	340	GP	do	.010	2.7		N.
W-2	341	GP	Bronchopneumonia; edema plus	.012	3.5		B.
W-2	342	GP	Normal	.008	2.6		N.
W-2	343	GP	Slight bronchopneumonia	.008	2.9		C.
W-2	344	Mo	Normal				
W-2	345	Mo	do				
W-2	346	Mo	do				
W-2	347	Mo	do				
W-3	351	Rb	Small area of bronchopneumonia	.006	1.6	.76	C.
W-3	352	Rb	Marked edema	.007	2.5	1.05	B.
W-3	355	GP	Pregnant; lungs and trachea normal	.011	3.0		N.
W-3	356	GP	do	.010	2.6		N.
W-3	357	GP	Normal	.013	3.5		N.
W-3	358	GP	do	.011	2.8		N.
W-3	363	Mo	do				N.
W-3	364	Mo	Slight patchy edema				C.
W-3	365	Mo	do				C.
W-3	366	Mo	Normal				N.
W-4	353	Rb	Moderate edema	.006	2.1	.9	B.
W-4	354	Rb	Marked edema	.012	3.8	1.5	A.
W-4	359	GP	Hemorrhages	(?)	3.3		C.
W-4	360	GP	Hemorrhages and atelectases	.015	3.3		C.
W-4	361	GP	Hemorrhages	.015	3.7		C.
W-4	362	GP	Hemorrhages and atelectases	.014	3.8		C.
W-4	367	Mo	Normal				N.
W-4	368	Mo	do				N.
W-4	369	Mo	do				N.
W-5	328	Rb	Extensive pneumonia and pleurisy		1.6		D
W-5	350	Rb	do	.012	4.5		D
W-5	383	GP	Hemorrhages; moderate edema	.016	3.8		B
W-5	384	GP	Moderate edema	.012	2.5		B.
W-5	385	GP	Pregnant; hemorrhages	.004	2.5		N.
W-5	386	GP	Normal	(?)	(?)		N.
W-5	327	Mo	Normal (?)				D.
W-5	387	Mo	Normal				
W-5	388	Mo	do				
W-5	390	Mo	Slight patchy edema				C.
W-6	391	Rb	Slight tracheitis; bronchitis	.007	2.7	.6	C.
W-6	398	Rb	Intense bronchopneumonia	.012	4.6	1.7	D.
W-6	392	GP	Slight edema; congestion	.02	3.8		C.
W-6	394	GP	Normal	.013	3.7		N.
W-6	407	OP	do	.012	3.0		N.
W-6	393	Mo	do				N.
W-6	395	Mo	do				N.
W-6	408	Mo	do				N.
W-6	389	Rb	Slight tracheitis; lungs normal		2.0		(?)
W-6	381	GP	Slight bronchopneumonia	.013	3.6		B. ¹
W-6	382	GP	Patchy edema; slight bronchopneumonia	.016	4.2		A. ¹
W-7	400	Rb	Normal; nasal discharge	.005	1.9	.6	N.
W-7	416	Rb	Normal	.004	1.6	.7	N.

¹ Control.

TABLE 97.—*Pathological report—Continued*

No. of experiment	Serial No.	Animal	Lesions	L/BW	L/H	L/K	Grade of casualty
W-7-----	401	GP	Normal.....	0.016	3.3	-----	N.
W-7-----	402	GP	Leucocytic infiltration of trachea; slight bronchitis.....	.014	3.7	-----	B.
W-7-----	407	GP	Normal.....	.008	3.8	-----	N.
W-7-----	403	Mo	No section.....	-----	-----	-----	N.
W-7-----	404	Mo	Normal.....	-----	-----	-----	N.
W-7-----	399	Rb	do.....	.005	2.0	0.7	N.
W-7-----	418	Mo	do.....	-----	-----	-----	N.
W-8-----	409	Rb	Bronchopneumonia.....	.005	2.1	.7	N.
W-8-----	410	Rb	Normal.....	.005	1.8	.7	N.
W-8-----	428	Rb	do.....	.005	2.2	.7	N.
W-8-----	411	GP	Bronchopneumonia.....	.013	3.3	-----	A.
W-8-----	412	GP	Slight bronchopneumonia.....	.015	3.6	-----	B.
W-8-----	429	GP	do.....	.014	3.7	-----	B.
W-8-----	(?)	Mo	Edema.....	-----	-----	-----	D.
W-8-----	413	Mo	Normal.....	-----	-----	-----	N.
W-8-----	414	Mo	do.....	-----	-----	-----	N.
W-9-----	406	Rb	Bronchopneumonia.....	-----	-----	-----	A.
W-9-----	419	Rb	Normal.....	-----	1.6	-----	N.
W-9-----	430	Rb	do.....	-----	2.0	-----	N.
W-9-----	420	GP	Bronchitis and slight bronchopneumonia.....	-----	3.0	-----	A.
W-9-----	421	GP	Bronchitis and bronchopneumonia.....	-----	3.8	-----	A.
W-9-----	431	GP	Bronchopneumonia.....	-----	3.2	-----	B.
W-9-----	422	Mo	Normal.....	-----	-----	-----	N.
W-9-----	423	Mo	do.....	-----	-----	-----	N.
W-9-----	432	Mo	do.....	-----	-----	-----	N.
W-10-----	424	Rb	Extensive pneumonia and pleurisy.....	-----	3.0	-----	A.
W-10-----	425	Rb	Tracheitis; lung normal.....	-----	1.7	-----	B.
W-10-----	433	Rb	Extensive bronchopneumonia.....	-----	2.1	-----	A.
W-10-----	426	GP	Bronchopneumonia.....	-----	3.2	-----	B.
W-10-----	427	GP	Scattered areas of bronchopneumonia.....	-----	4.2	-----	A.
W-10-----	434	GP	Bronchopneumonia.....	-----	4.8	-----	A.

DISCUSSION

1. In all experiments with the varying concentrations tried, a large proportion of both rabbits and guinea pigs showed pulmonary lesions, usually a bronchopneumonia of greater or lesser extent, but in a few cases simple edema. The remaining animals were normal grossly and histologically.

2. It is doubtful whether the respiratory lesions observed can be attributed to the inhalation of the dimethyltrithiocarbonate, since: (1) A number of stock rabbits, dying spontaneously about the time the experiments were being conducted, showed respiratory infections with lesions similar to those in the experimental animals.

(2) Two guinea pigs killed with hydrocyanic acid as controls, showed bronchopneumonia lesions of moderate severity, similar to those in many of the exposed animals.

(3) Only 4 mice out of 26 exposed showed pulmonary lesions, and these were trifling. Such a relative species immunity in the case of mice would be highly exceptional.

3. It can not be definitely stated, on the other hand, that the exposure to the toxic gas did not predispose to subsequent infection. This possibility is borne out by the fact that in a small proportion of the cases edema, with little or no inflammatory exudation into the alveoli, was found—a type of lesion difficult to attribute to spontaneous infection.

4. It would be desirable to carry on further experiments, using sounder stock and carrying the observation over a longer period.

SPECIAL REPORT NO. 15. THE BEHAVIOR OF CERTAIN SLUGS AND SNAILS IN THE PRESENCE OF DICHLORETHYLSULPHIDE

A telegraphic request was received to apply tests on the French species of the common European snails and slugs, since recent laboratory reports indicated that such animals were very sensitive to dichlorethylsulphide, reacting to it in a concentration of 2 parts per million.

Laboratory facilities were not at hand at the time the request was made, so a preliminary study was made under circumstances somewhat similar to field conditions.

The specimens employed were the common red, forest slug (*Arion rufus*) and the common white, edible type of snail (*Helix aspersa*). The experiment was conducted as follows: (a) Direct application of the crude mustard oil from a German shell to an area on the dorsal and ventral surfaces of 3 slugs and 3 snails. (b) Exposure of 12 slugs and 12 snails to the vapor of the same substance. (c) Notes on these animals with regard to such common factors as smoke, concussion, rapid changes in temperature and lights, as well as the character of the materials upon which they may be placed.

DIRECT APPLICATION OF DICHLORETHYLSULPHIDE

The red slug was touched with a droplet of crude dichlorethylsulphide on the dorsal and ventral surfaces near the cephalic end. Immediately there began a slow general contraction of the entire body and an abundant secretion of transparent, viscid fluid which dried on the fingers of the examiner very much as does collodion. This secretion very quickly formed a large drop at the point where the dichlorethylsulphide was applied. Aside from this local feature there did not appear, either early or late, any local change such as a marked change in color, edema, ulceration, or exfoliation. The slugs were all somewhat shrunken in size, and a general change in color from a yellowish-red to a brownish-red took place after several hours had passed. This may have been due simply to the contracted state of the body, for at a later observation they approached their normal color. At the end of two weeks there was nothing more to be noted.

The white snail was treated in the same way as the red slug. Upon application of the dichlorethylsulphide, it immediately drew its body well back into its shell, leaving a ball of transparent, foamy, viscid material closing the entrance. It was easily made to retract and disappear in its shell by simple irritation with a straw or other foreign body, but the secretion mentioned was rather remarkable. Evening and daytime observations during the next three days failed to find any of them protruding from the shell, but thereafter they appeared in the evenings or when placed in a shaded, moist, grassy spot. They did not make as long an excursion as usual, however. At the end of three weeks all were still alive and revealed only a slight brownish-yellow pigmentation on the ventral surface.

EXPOSURE TO VAPOR OF DICHLORETHYLSULPHIDE

A tight wooden box of about one-quarter cubic meter capacity was employed. It was closed with a roof made of gelatin-filled cordon wire, and over the grass-covered ground floor was fixed a screen wire (not filled with gelatin) which rested a few centimeters above the ground. Over this were scattered some fresh twigs and leaves. Before adjusting this floor and admitting the animals about 15 c. c. of crude dichlorethylsulphide was scattered over the ground. In this way the snails were exposed to the vapor of dichlorethylsulphide under somewhat modified field conditions. The red slugs showed more or less activity during the first few hours, but the following day most of them were quiet and hidden away in the leaves, even late in the evening. Two were found in direct contact with the wire screen floor, and these were shrunken in size and of a reddish-brown color. These slugs, when released at the end of three days, were able to crawl away except for the pair found lying directly on the screen floor. The common white edible snails, when tested under the same conditions, rather slowly withdrew into their shells, leaving a foamy, viscid, transparent ball of fluid covering the shell hole. The following morning a few of those among the leaves had reappeared, and the exposed portions of body margins, as well as the ventral surface, were discolored a yellowish-brown and covered with a turbid film. At the end of two days they were removed and placed on a moist block of wood covered with a screen cage that would permit short excursions over grass about the block. During the three weeks these snails were under observation only two or three left the block, and very few appeared from the shell in so far as evening observations were concerned. By touching them with a straw they would quickly recede to a greater depth in the shell. Between 10 days and 3 weeks afterwards all had died. The ventral surface, margins, and scattered local areas were dry, brown, and hard.

OTHER NOTES

It was found during the course of this study that these animals reacted easily to many factors. Their movements when exposed to dichlorethylsulphide were quite like those due to common irritation such as exposure to tobacco smoke, sudden extreme changes in temperature, and light, jarring, strong winds, etc. It would appear unsafe, therefore, to place too much reliance on their immediate behavior when placed in the presence of field concentrations of dichlorethylsulphide.

SUMMARY

The red forest slug (*Arion rufus*) is much more resistant to dichlorethylsulphide action than the snail (*Helix aspersa*). The above experience does not indicate that these snails and slugs can be made use of as field indicators for dichlorethylsulphide.

SPECIAL REPORT NO. 44, A SUIT FOR PROTECTION AGAINST MUSTARD GAS

The suits used in these experiments were made of two layers of "canaburg," a loosely woven cotton fabric, the outer layer of which was impregnated with simplexene B (45 parts rosin, 55 parts rosin oil).¹⁴ The prepared fabric was quite freely permeable to air, and the suit did not interfere with heat loss from the body to the same extent as do the impermeable suits hitherto used.

It was not anticipated by the designers that the fabric would protect against liquid dichlorethylsulphide; consequently the first experiments dealt solely with protection against vapor. Before submitting the suits to extensive trial at the front request was made for data concerning the possibility of protection against the liquid, and certain of the experiments herein recorded dealt with the possibility of protection against liquid and spray.

The conclusions which the experiments appear to justify follow:

EXPERIMENTS AGAINST VAPOR OF DICHLORETHYLSULPHIDE

HORSES' SKIN

The horse's skin was completely protected by suit fabric from 15 minutes' exposure to saturated dichlorethylsulphide vapor at about 13° C. Protection was not complete against 25 and 30 minutes exposure at 11° C. Wet suit fabric was somewhat less protective than dry. (Experiments 1-5.)

HUMAN SKIN

By the static method of testing, human skin was completely protected against 20 minutes' exposure to air saturated with dichlorethylsulphide vapor. Protection was almost complete against 40 minutes' exposure. By another method of testing, complete protection against an hour's exposure to a high concentration was obtained. (Experiments 6-9.)

IN CHAMBER EXPOSURE

Partial protection was afforded to persons wearing the protective suit in nominal concentrations of 1 to 100,000, 1 hour, and 1 to 31,000, 30 minutes. Protection was least adequate for the scalp, scrotum, and inner surface of thighs. (Experiments 10-13.)

ABSORPTION OF DICHLORETHYLSULPHIDE BY PROTECTIVE FABRIC

More dichlorethylsulphide was absorbed by the protective fabric than by khaki cloth when both were suspended in air saturated with dichlorethylsulphide vapor. (Experiments 14 and 15.)

PROTECTION AGAINST LIQUID DICHLORETHYLSULPHIDE

One layer of suit fabric, the outer surface of which was wet with yellow cross shell filling, might remain in contact with the horse's skin for between 16 and 30 minutes without causing lesions. (Experiment 16.)

When the suit fabric, in direct contact with human skin, was sprayed with yellow cross shell filling, it might remain in contact for 10 minutes in some cases without producing lesions. In other cases erythema was produced by contact of this duration. Severe reaction was apt to be produced by contact of 2 to 30 minutes.

When the suit fabric, placed over the other clothing (blouse, shirt, and undershirt), was similarly sprayed, it might remain in contact for 30 minutes in some cases without producing reaction. Experiment 20 indicates that sensitive persons would be injured in such a test. (Experiments 18-22.)

One subject, fairly insensitive to dichlorethylsulphide was completely protected during 50 minutes in which he was enveloped for from 30 to 60 seconds

in the visible clouds produced by separate explosions of six 75-mm. dichloroethylsulphide shells. Another subject, decidedly more sensitive to dichloroethylsulphide, developed mild erythema as the result of the same exposure. (Experiments 23 and 24.)

When 600 c. c. of yellow cross shell filling were dispersed in a manner closely similar to that in which it was dispersed when a German 77-mm. yellow cross shell was exploded at rest, men wearing the protective suits, together with boots, gloves, helmets, and respirators, might stand 4 to 6 paces away from the explosion, receive liberal spattering of spray and droplets, wear the suits for a further period of from 20 to 60 minutes, and not be injured seriously. This conclusion was based on three experiments in which eight persons were exposed. The length of time during which a person might safely wear the suit after such exposure obviously depended on the quantity of shell contents with which he was spattered, and judgment was necessary in applying this conclusion to comparable field exposures. (Experiments 25-27.)

Men wearing the protective suit, together with boots, gloves, helmets, and respirators, might walk through woods which had been heavily shelled with yellow cross for from 20 to 30 minutes, and might keep the suits on while working for another 30 minutes with a fair chance of escaping injury. If too great confidence were placed in the protective power of the suit serious casualty might result. (Experiments 28-29.)

After being contaminated by shell burst or by contact with undergrowth in woods shelled with yellow cross, the protective suit might retain dangerous amounts of dichloroethylsulphide for as long as 48 hours and doubtless longer. It would be unwise to wear it as long as it gave off the odor of dichloroethylsulphide. (Experiments 30-31.)

SUMMARY OF CONCLUSIONS

On the basis of these conclusions it was thought that the protection afforded by this suit might enable men to work for several hours without serious danger on open ground heavily contaminated with dichloroethylsulphide; to walk for half an hour through thick woods which had been heavily shelled with yellow cross, or for a longer time if the woods were open or if they had been lightly shelled. If a man wearing the suit should be heavily spattered with dichloroethylsulphide from a shell burst, or if the fabric became actually wet with dichloroethylsulphide from any cause, the suit should be removed as soon as possible.

EXPERIMENTS

AGAINST VAPOR OF DICHLORETHYLSULPHIDE

ON HORSES' SKIN

Air saturated with vapor of dichloroethylsulphide at outdoor temperature was applied to the shaved skin of a horse. A layer of the suit fabric was interposed between the mouth of the bottle containing cotton wet with dichloroethylsulphide and the skin. In some control tests, khaki cloth was used instead of the protective cloth; in other controls the vapor was applied directly to the skin.

EXPERIMENT 1.—Vapor from pure dichlorethylsulphide, and from yellow cross shell fillings; temperature, 13.5° C.; exposure, two hours. Skin protected by one layer of suit fabric. *Result*.—Severe reaction began to develop in both tests 15 minutes after exposure.

EXPERIMENT 2.—Vapor from pure dichlorethylsulphide; temperature, 9° C.; exposure 30 minutes. (a) Skin protected by one layer of suit fabric. (b) Skin protected by one layer of khaki. (c) Skin unprotected. *Result*.—The reaction which developed in (a) was distinct but decidedly less than that in (b) or (c).

EXPERIMENT 3.—Vapor from pure dichlorethylsulphide; temperature, 12.8° C.; exposure 15 minutes. (a) Skin protected by suit fabric. (b) Skin protected by khaki. (c) Skin unprotected. *Result*.—No reaction in (a); definite reactions in (b) and (c).

EXPERIMENT 4.—Vapor from pure dichlorethylsulphide; temperature, 11° C. (a) Skin protected by suit fabric; exposure, 25 minutes. (b) Skin unprotected; exposure, 5 minutes. *Result*.—Reaction in (b) slightly greater than in (a). The reactions were of the same order.

EXPERIMENT 5.—Vapor from pure dichlorethylsulphide; temperature, 11° C.; exposure, 15 minutes. (a) Skin protected with suit fabric which was thoroughly wet with water. (b) Skin protected with khaki. (c) Skin unprotected. *Result*.—Slight reaction developed in (a); definite reactions developed in (b) and (c).

ON HUMAN SKIN

EXPERIMENT 6.—Subject R. Exposure of forearm to saturated vapor at 9° C. Static method. (a) Skin protected with suit fabric; exposure, 20 minutes. (b) Skin protected with khaki; exposure, 10 minutes. (c) Skin unprotected; exposure, 10 minutes. *Result*.—No reaction in (a). Erythema in (b) and (c).

EXPERIMENT 7.—Subject G. Saturated vapor at 9° C. Static method. (a) Skin protected with suit fabric; exposure, 40 minutes. (b) Skin protected with khaki; exposure, 15 minutes. (c) Skin unprotected; exposure, 10 minutes. *Result*.—Very slight erythema in (a). Marked erythema in (b) and (c).

EXPERIMENT 8.—Subject G. The whole forearm was protected by two layers of the suit fabric except at one spot 1½ inches in diameter where one layer was cut away. For 30 minutes it was held in a large tin box in which an excess of liquid dichlorethylsulphide had been placed and warmed with an alcohol lamp. *Result*.—No reaction developed.

EXPERIMENT 9.—Subject R. Forearm, protected as described under experiment 8, was held for one hour in tin box containing dichlorethylsulphide vapor. Liquid dichlorethylsulphide had been standing in a shallow dish within the box for 16 hours. *Result*.—No reaction developed.

CHAMBER EXPERIMENTS

(a) Concentrations of dichlorethylsulphide were raised in a chamber of 19.7 cubic meters capacity. The walls of the chamber were covered with "beaver board" and doubtless absorbed a portion of the vapor. The actual concentrations were probably materially lower than calculated.

(b) Subjects exposed in the chamber wore the protective suit over all their other clothing except the blouse, which was not worn. The shirt sleeves of one arm were rolled above the elbow and a small circular hole was cut through the protective sleeve, so that a circle of unprotected skin was exposed.

(c) Protective boots, gloves, and the small box respirator were also worn.

(d) Concentrations were raised by heating pure dichlorethylsulphide in a casserole by an alcohol lamp. The subjects were in the chamber during the 19 minutes or more necessary for evaporating the dichlorethylsulphide, but recorded times of exposure refer to time after the concentrations were raised.

(e) Two rabbits were exposed in the chamber during each experiment.

EXPERIMENT 10.—Subjects R and G. Nominal concentration of dichlorethylsulphide, 1 to 100,000, raised by heating 1.1 e. e. purified dichlorethylsulphide. Time of exposure, 1 hour. *Result*.—No unmistakable erythema of exposed spot on right forearms. Distinct

erythema appeared about old dichlorethylsulphide scars on the protected left arm of one subject. Rather severe itching of old dichlorethylsulphide scars was noted by both subjects during the evening following exposure. One rabbit showed severe conjunctivitis the following morning; the other showed little.

EXPERIMENT 11.—Subjects R and G. Nominal concentration 1 to 31,000, raised by heating 3.5 c. c. purified dichlorethylsulphide. Time of exposure, 30 minutes. R wore same suit as in experiment 10; G wore a new suit. *Results*.—Very faint erythema of exposed spot on right arm in both subjects. Annoying irritation of old dichlorethylsulphide scars on left arm, of scalp, and of scrotum was experienced during evening following exposure. G developed slight erythema of forehead above line of face mask of respirator. Both rabbits showed severe conjunctivitis 18 hours after exposure; 24 hours later excessive nasal discharge was noted.

EXPERIMENT 12.—Subjects R and D. Subject D is known to be more sensitive to dichlorethylsulphide than either R or G. Nominal concentration, 1 to 31,000. Exposure, 30 minutes. Unprotected areas on right arm larger than in previous experiments. R wore same suit as in two previous experiments. D wore G's suit of experiment 10. *Result*.—Subject D: Seven hours after exposure severe itching of scalp, body, and thighs began. Areas about old dichlorethylsulphide scars and scrotum were especially annoying. Twenty hours later erythema of unprotected spot on right arm was distinct. There was slight erythema of scalp, inner surface of thighs, and of scrotum. Irritation was such as to prevent sleep for two nights but no blistering occurred. Subject R: Erythema of exposed spot on right arm. Annoying itching of scalp, scrotum, and inner surface of thighs. Both rabbits developed very severe conjunctivitis and purulent nasal discharge.

EXPERIMENT 13.—Subjects R and K. (K is known to be extremely sensitive to dichlorethylsulphide.) Nominal concentration, 1 to 31,000. Exposure, 30 minutes. Subject R wore a pair of trunks cut from another protective suit in addition to the protective suit itself. *Result*.—Subject R: Aside from slight irritation of the scalp, protection was complete. Subject K: Erythema of exposed spot on right forearm developed in three hours; it was intense on the following day. Diffuse erythema of right forearm, left wrist, neck, and forehead. The skin of neck became swollen, but no blistering occurred.

ABSORPTION OF DICHLORETHYLSULPHIDE BY THE SUIT FABRIC

EXPERIMENT 14.—Immediately after coming out of the chamber concentration in experiment 12, pieces of cloth were cut out of the sleeve of the suit worn by R and bound to the unprotected skin of the forearm of subject G and worn for one and one-half hours. *Result*.—No reaction developed.

EXPERIMENT 15.—Pieces of khaki cloth and of protective fabric were suspended in a jar containing air saturated with dichlorethylsulphide vapor for 30 minutes. Small circles of each were cut out and bound on the forearms of two persons and worn for two hours.

PROTECTION AGAINST LIQUID DICHLORETHYLSULPHIDE

HORSE'S SKIN

EXPERIMENT 16.—The skin was shaved, washed with soap and water and alcohol, and dried. One layer of protective fabric was laid over the shaved area, and over this was placed a layer of impermeable fabric in which five holes had been cut, each $1\frac{1}{2}$ inches in diameter. German yellow cross shell filling was sprayed with an atomizer so that the exposed circles of protective fabric were actually wet. The impermeable fabric was removed at once. The wet circles of protective fabric were cut away after contact with the skin for 5, 10, 15, 30, and 60 minutes, respectively. Temperature was 12° C. *Result*: Contact for 5, 10, and 15 minutes caused no reaction. Contact for 30 minutes caused a slight reaction. Contact for 60 minutes caused a severe early reaction, which receded decidedly during following 24 hours.

HUMAN SKIN

EXPERIMENT 17.—Subject R. The forearm, bare save for a layer of suit fabric, covered by impermeable fabric in which were cut four holes, each 1 inch in diameter. German yellow cross shell filling was sprayed by an atomizer directly against the exposed protective fabric. One circle was cut away after contact for 1 minute, the others after 2, 5, and 10 minutes' contact, respectively. *Result*.—No reaction developed.

EXPERIMENT 18.—Subject R-2. Like experiment 17. Contact with sprayed suit fabric for 10, 20, and 30 minutes. *Result*.—All three exposures gave moderate erythema, but no blistering.

EXPERIMENT 19.—Subject G-2. Like experiment 17. Contact with sprayed suit fabric for 10, 20, and 30 minutes. *Result*.—Ten minutes' contact caused erythema; 20 and 30 minutes' contact caused erythema followed by blistering, which was severe in the case of the 30-minute exposure.

EXPERIMENT 20.—Subject R (known to be extremely sensitive to dichlorethylsulphide). Suit fabric placed on arm over O. D. shirt sleeve and woolen undershirt sleeve. Sprayed with yellow cross shell filling as in experiment 17. Contact for 10, 15, and 20 minutes. *Result*.—Diffuse erythema over whole forearm developed in 5 to 7 hours, which was most severe at points directly under sprayed areas. Erythema spread up the arm and shoulder. The arm became much swollen, and the swelling persisted for about 5 days. A blister developed on the area where contact lasted 20 minutes.

EXPERIMENT 21.—Subject R. Forearm covered by blouse, shirt, and undershirt. Suit fabric, laid over these, sprayed as in experiment 17. (Contact for 10, 20, and 30 minutes.) *Result*.—No lesions.

EXPERIMENT 22.—Subject W. Like experiment 21. Contact 30 minutes. *Result*.—Very slight erythema.

EXPOSURE TO CLOUDS FROM YELLOW CROSS SHELL BURSTS

EXPERIMENT 23.—Two subjects (C and V) wearing protective suits, boots, gloves, and respirators, ran into the cloud produced by exploding a 75-mm. dichlorethylsulphide shell at rest. They walked about the crater for 1 to 2 minutes. The suits were then removed. *Result*.—No lesions.

EXPERIMENT 24.—Two subjects (R and C), wearing protective suits, boots, gloves, and respirators, ran into the cloud produced by each of six 75-mm. dichlorethylsulphide shells exploded singly at intervals of about 10 minutes. They were in the visible cloud from each shell for from 2 to 10 seconds and walked about the crater of each shell for from 1 to 2 minutes after the cloud had disappeared. The suits were worn for a total of 50 minutes. *Result*.—Subject R developed no lesions. Subject C: Erythema developed in about 3 hours on arm, trunk, knees, and scrotum. No blisters. Erythema persisted for 48 hours.

EXPOSURE TO SPRAY FROM SHELL BURSTS*

EXPERIMENT 25.—The contents of a German 77-mm. yellow cross shell (600 c. c.), contained in a tin can, were dispersed by detonating the picric acid gained from the same shell immersed in the liquid. In this way the explosion of a 77-mm. yellow cross shell was reproduced without danger from shell fragments. Three subjects, R, B, and V-2, wearing protective suits, boots, gloves, helmet, and respirator, stood 6 paces down wind from the "shell." The shell contents were distributed as a cloud of small droplets and fine spray, which enveloped the subjects. Subjects R and V-2 were well sprinkled about left arm, shoulder, and back; only slightly sprinkled below the waist. Subject B was well sprinkled from head to foot. B removed his protective clothing 15 minutes after the burst; V-2, 18 minutes after burst; R, 22 minutes after. Other clothing which had been worn during the test was kept on during the rest of the day. *Result*.—No lesions in any subject.

EXPERIMENT 26.—The contents of a German 77-mm. yellow cross shell (600 c. c.) were dispersed exactly as in experiment 25. Wind velocity was 7 m. p. s. Three subjects, B-2, C-2, and W, wearing protective clothing, respirators, and helmets, crouched 6 paces down wind from the "shell." Subject B-2 was liberally sprinkled from head to foot. C-2 was well sprinkled over left arm and side. W was well sprinkled about the waist. B-2 wore his protective clothing for 20 minutes, C-2 for 30 minutes, and W for 40 minutes after the burst. Other clothing worn during exposure was kept on during the rest of the day. *Result*.—Subject B-2 showed slight erythema of back, arm, and scrotum, which began 4 hours after exposure and persisted several days. Irritation was not sufficient to prevent sleep. Subjects C-2 and W developed moderate erythema of back, which persisted for several days, but which caused very little annoyance.

* In experiments 25 to 29 Capt. W. A. Bush, R. E., rendered valuable assistance. He devised and carried out the experiments with shell bursts, the effects of which were studied.

EXPERIMENT 27.—Like experiments 25 and 26. Two subjects, R and V-2, wearing protective clothing, stood 5 paces down wing from "shell" containing 400 c. c. yellow cross shell filling. Another explosion of 300 c. c. of yellow cross shell filling was immediately arranged, the subjects standing 4 paces away. Both subjects were scantily sprinkled. Protective clothing was removed one hour after the first explosion. *Result*.—Neither subject developed any lesion.

EXPERIMENTS IN WOODS HEAVILY SHELLLED WITH YELLOW CROSS

EXPERIMENT 28.—A wooded area, roughly pentagonal in shape and including about 4,000 square feet, was wired off. Except for a small space in the center it was densely covered with small beech saplings, scrub oak, and thorn bushes. It was impossible to walk about in the area without constantly brushing against the twigs and branches. A 150-mm. German howitzer yellow cross shell was exploded in the center of the area. Temperature was 13° C. and wind 2 meters per second. Eighty minutes later, three subjects, R, V-2, and H, wearing protective clothing, boots, gloves, helmets, and respirators, entered the area and walked for 20 minutes, taking pains to go through the thickest undergrowth. On emerging, they removed respirators and helmets and threw back the hood of the suit. The protective suit was worn during a further walk of half an hour and then removed. The temperature during exposure and the subsequent walk was 15° to 16.5° C. and the air was very humid; all three became very sweaty. The other clothing worn during the test was kept on during the rest of the day. No precautions were taken other than washing face and hands after removing protective clothing. *Result*.—No lesions in any subject.

EXPERIMENT 29.—On the day following experiment 28, another 150-mm. German howitzer yellow cross shell was exploded in the same place. Temperature 8.5° C.; no wind; fairly heavy fog. Thirty minutes later, three subjects, W, H, and V-2, wearing protective suits, etc., entered the area. They walked about for one hour, taking pains to rub against the undergrowth and to force their way between the trunks of closely set saplings. One subject (W) stated that whenever he saw a black splash on a tree or bush he rubbed against it. On emerging respirators were removed, but the protective clothing was worn during a further walk of 25 minutes. All became very hot, sweaty, and uncomfortable. On removing protective suits, hands and faces were washed; no other precautions were taken. *Result*.—Five hours after exposure, subjects W and H showed marked erythema of shoulders, buttocks, thighs, and knees. Subject V-2 showed no lesion. All bathed thoroughly with warm water and soap. Some of the erythematous areas were treated with 1 per cent potassium permanganate solution. Twenty hours later W has a large blister on right shoulder, a small blister on left wrist, small blisters about the penis, erythema of back, buttocks, thighs, serotum, and knees. H had large blisters on back and shoulder, small blisters on serotum, erythema of buttocks, thighs, and knees. Slight erythema of portion of face covered by respirator mask. V-2 had no lesions. W and H were sent to the hospital.

SUBSEQUENT DANGER FROM THE PROTECTIVE SUITS AFTER CONTAMINATION WITH LIQUID DICHLORETHYLSULPHIDE

EXPERIMENT 30.—One of the suits worn in experiment 25 gave distinct odor of dichlorethylsulphide six hours after the experiment. In the meantime it had been hanging in a large airy building. A small piece of cloth was cut from it, bound to arm of subject R, and worn for 4 hours. *Result*.—Marked erythema had developed before it was removed, and a blister appeared two days later.

EXPERIMENT 31.—Twenty-four hours after experiment 29, a piece of the fabric from one of the suits worn in that experiment, which still gave distinct odor of dichlorethylsulphide, was bound to the arm of subject D, and worn for an hour. *Result*.—It produced erythema, but no blister.

Forty-eight hours after the experiment another piece was cut from the same suit, still giving the dichlorethylsulphide odor, bound to the arm of subject R and worn for four hours. *Result*.—Erythema developed during the four hours, and severe blistering occurred subsequently.

The suit, during the 48 hours following the experiment, was hanging in a large airy building.

SPECIAL REPORT NO. 49. THE PROTECTIVE POWER OF SAG PASTE, CALCIUM HYPOCHLORITE OINTMENT, AND PETROLATUM AGAINST DICHLORETHYLSULPHIDE AND LEWISITE I

The value ascribed by some observers to sag paste and other ointments as protection against dichlorethylsulphide and the dissenting views held by others, led, in view of the practical importance of the subject, to the making of some independent observations. The ointments tested were: (1) Sag paste (zinc stearate); (2) calcium hypochlorite (10 per cent in white petrolatum, U. S. P.); (3) petrolatum (unmedicated). The first named was chosen because it had been selected officially for extensive field tests. Calcium hypochlorite ointment had been found effective experimentally by the French and English. Petrolatum, on the other hand, had been found useless or positively deleterious.

The first experiments were made on the skin of the horse, using alcoholic solutions of dichlorethylsulphide of various concentrations. This method was tried in the hope of obtaining a numerical expression of degree of protection. In later experiments on the horse and on man the static method of exposure to saturated dichlorethylsulphide vapor was employed. In the experiments on man, exposures to Lewisite I were included.

EXPERIMENTS ON THE SKIN OF THE HORSE

Three tests were made to determine the protection afforded by sag paste, calcium hypochlorite ointment, and petrolatum against solutions of dichlorethylsulphide in absolute alcohol. In the method employed, a definite constant amount of dichlorethylsulphide to be evenly applied to a constant known area of the skin with which it was left in direct contact by the evaporation of the alcohol in which it was dissolved. In the first experiment the efficacy of sag paste was estimated by the application of varying percentages (2 and 3 per cent) of dichlorethylsulphide to treated and control areas. With the 1 per cent solution no difference was noted between sag paste and control areas; with the 2 per cent and more definitely with the 5 per cent solution the treatment by sag paste delayed the onset of swelling and, up to 24 hours, retarded its full development. At 48 hours and subsequently the reaction in all areas was practically identical.

In the second experiment sag paste was compared with petrolatum; the former again retarded the onset of reaction to percentages of dichlorethylsulphide above 1 per cent when compared with petrolatum, but this favorable effect was not noticed at the end of 24 hours or subsequently.

In a third experiment calcium hypochlorite ointment was compared with petrolatum, but no difference in the lesions produced by the dichlorethylsulphide was observable. When, however, a definite percentage of dichlorethylsulphide was added to calcium hypochlorite ointment and petrolatum, respectively, and weighed amounts of these ointments were applied to the skin of the horse, the former caused much less swelling and induration than the latter. This effect, however, was clearly due to a direct chemical breaking down of the dichlorethylsulphide and not to a true protective action.

Series II.—Since the application of solutions gave such inconclusive results, the effect of dichlorethylsulphide vapor was then tried. Vapor tests have the added advantage of simulating more or less closely conditions likely to be met with in the field. Experiments 4 and 5 were devoted to determining

the most suitable technique, under the circumstances, for applying vapor by the "static" method, and particularly the optimum time of exposure. With the temperature at 20° C. or thereabouts an exposure of 5 minutes is sufficient to produce a definite lesion in 24 hours or less, but if the temperature of the air is much below 15° C. it is better to prolong the exposure to 7 or 10 minutes or to make use of a water jacket (at 20° C.). Experiments 6, 7, 8, and 9 were performed successively to determine the protective value of sag paste and petrolatum against saturated dichlorethylsulphide vapor, using untreated skin areas for controls. In experiments 6 and 7 the ointments, irrespective of their composition, seemed to favor a more prompt reaction to the dichlorethylsulphide, while in 8 and 9 even this distinction between the exposed areas was absent. In experiment 9 the ointments were washed off with soap and water five minutes after the exposure to dichlorethylsulphide, but this did not delay or prevent the swelling and induration. While the tabulated (early) results were unfavorable to both ointments, yet subsequently the sag paste areas (experiments 6 and 7) seemed less swollen and indurated than the remaining areas. Other tests (experiments 10 to 14) intended to determine the protective value of hypochlorite ointment, etc., were also negative.

Series III.—Up to this time one horse had been employed. In order to test further the effects of the ointments mentioned and to exclude the influence of idiosyncrasy, the experiments were repeated in two other horses, one with a highly sensitive skin, the other with a tough leathery hide. The results of experiments 15 to 18 were inconstant, though both sag paste and hypochlorite ointment seemed at times to afford slight protection when judged by the lesions at 24 hours. Petrolatum on the other hand seemed to be constantly devoid of protective powers. Further tests of hypochlorite ointment (experiments 19 and 20) were negative.

It was concluded that the protective ointments which were examined are of little or no value in protecting the skin of the horse against solutions of dichlorethylsulphide or against air saturated (20° C. approximately) with dichlorethylsulphide vapor. Whatever value sag paste may have in this connection is manifested either by delaying the onset of symptoms or in slightly modifying their severity.

Experiments in man to test the protective action of sag paste, calcium hypochlorite ointment, and petrolatum against dichlorethylsulphide, and, incidentally, against Lewisite I vapors.

In experiment 29, five individuals with varying susceptibility to dichlorethylsulphide and Lewisite were tested by the vapor or static method, using very small tubes. For the untreated or control areas and the areas treated with petrolatum an exposure of 10 minutes was allowed; for sag paste 15 minutes; for hypochlorite ointment 20 minutes. The intention was to secure distinct lesions in each instance without causing undue vesiculation in the central areas. In estimating the results, due allowance was made for the difference in exposure. Details of technique and tables are given below. From these tests the general conclusion was drawn that sag paste and hypochlorite ointments afforded moderate protection against the vesicant vapors tested which was only absolute when the control lesions were minimal. Petrolatum was found to be either indifferent or positively deleterious. Further tests with this substance were therefore deemed unnecessary, particularly as this finding is in agreement with the observations of others.

In experiments 30 and 31, three individuals tested in each instance, the technique was slightly altered in that larger tubes were employed and the exposures were made uniform and simultaneous. The new sag paste issued by the Purchase and Supply Division of the Chemical Warfare Service was used in these tests. Here again sag paste gave moderate protection against dichlorethylsulphide in nearly three-fourths of the tests and against Lewisite in about one-half of the tests. The results with hypochlorite ointment were similar but less uniform; sometimes the protection was very marked, while in other instances the action of the vesicant was intensified.

CONCLUSIONS

(a) In man, therefore, both sag paste and hypochlorite ointment afford a certain degree of protection against the vesicant vapors under consideration; this is seldom or never absolute and is entirely absent in one-third to one-half the cases. Sag paste is preferable, as it is certainly nonirritating and probably more permanent than the hypochlorite ointment.

(b) In testing the relative value of protective substances it is necessary to use human skin. While the skin of the horse is more sensitive, it is probable that minor effects are missed since erythema if present can not ordinarily be distinguished.

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APPENDIX

APPENDIX

SUMMARY OF PRODUCTION, FIELD SUPPLY SECTION, GAS DEFENSE SERVICE ^a

[Weekly report. June 29, 1918]

	Total to May 21, 1918	Through June 29	Total to June 29, 1918
Respirators:			
Export.....	950,402	494,391	1,444,793
Tissot.....	1,261	5,925	7,186
Training.....	257,732	380	258,112
Experimental.....	4,908	3,633	8,541
Total gas masks.....	1,214,303	504,329	1,718,632
Horse masks.....			154,094
Trench fans.....			11,200
Gas samplers.....			1,000
Oxygen inhalators.....			1,202
Bleaching powder, tons.....			112

Comparative statement of production, deliveries, and shipments of gas masks

Production of export masks through June 29, 1918:

Gas defense plant.....	617,437
Hero Manufacturing Co.....	827,356
Total.....	1,444,793

Deliveries to quartermaster for overseas shipment to June 29, 1918, inclusive:

Gas defense plant.....	622,274
Hero Manufacturing Co.....	802,198
Total.....	1,424,472

Shipments overseas to June 28, 1918, inclusive:

Gas defense plant.....	391,464
Hero Manufacturing Co.....	805,323
Total.....	1,196,787

Additional deliveries to quartermaster:

Extra canisters with canister cartridges attached (to June 29, inclusive)....	297,534
Extra canisters without canister cartridges attached (to June 28, inclusive)...	141,150

Production of training masks through June 29, 1918:

Gas defense plant.....	1,040
Hero Manufacturing Co.....	257,072
Total.....	258,112

Production of experimental masks through June 29, 1918:

Gas defense plant.....	4,058
Hero Manufacturing Co.....	4,483
Total.....	8,541

Horse masks:

To be furnished.....	350,000
Manufactured to date.....	154,094
Delivered to quartermaster to June 29, 1918.....	145,750

^a Final weekly report. Taken over by the Chemical Warfare Service on July 1, 1918. Copy on file, Historical Division, S. G. O.

Trench fans:

To be furnished.....	15, 000
Delivered to quartermaster for shipment overseas.....	9, 600
Delivered to various camps for training purposes.....	1, 600
Total.....	11, 200

Oxygen inhalators:

To be furnished.....	1, 300
Supplied to France, through quantity requested.....	1, 000
Delivered to various camps for training purposes.....	125
In storage at gas defense plant.....	77
In process of manufacture.....	98

Total delivered, in storage, and in process..... 1, 300

Bleaching powder delivered to quartermaster to June 29, 1918, tons..... 112

Chemical equipment for gas houses at training camps: The gas houses at all cantonments have been supplied with the necessary chemicals for training purposes, and further supplies are being issued as requisitioned.

Miscellaneous equipment: The several items of miscellaneous equipment are being cared for.

APPENDIX

INSTRUCTORS IN GAS DEFENSE METHODS, FIELD TRAINING SECTION, GAS DEFENSE SERVICE^a

Document No. 4.

Washington, D. C.:

Capt. James H. Walton, officer in charge, field training section, Gas Defense Service.

Lieut. Ellery K. Files.

Lieut. George W. Keitt.

Maj. S. J. M. Auld, chemical adviser, British Military Mission.

DIVISIONAL GAS DEFENSE SCHOOLS NATIONAL ARMY

Camp and location	Divisional gas officer	Chemical adviser	British adviser
Custer, Battle Creek, Mich.....	Lieut. F. P. Nevins, M. R. C.....	Lieut. G. M. Bishop.....	Capt. W. Algie.
Deveus, Ayer, Mass.....	Lieut. Smith, M. R. C.....	Lieut. F. L. Conover.....	Capt. J. W. Turner.
Dix, Wrightstown, N. J.....	Capt. F. R. Illsley, M. R. C.....	Lieut. R. F. Smith.....	Lieut. W. J. Howieson.
Dodge, Des Moines, Iowa.....	Capt. H. C. Woltman, M. R. C.....	Lieut. V. L. Bonson.....	Capt. J. H. Brightman.
Funston, Fort Riley, Kans.....	Capt. R. B. Irones, M. R. C.....	Lieut. H. D. Valentine.....	Capt. J. E. Few.
Gordon, Atlanta, Ga.....	Capt. F. L. Benz, M. R. C.....	Lieut. T. B. Downey.....	Capt. C. H. Daniels.
Grant, Rockford, Ill.....	Capt. J. H. Sweeney, M. R. C.....	Lieut. L. M. Henderson.....	Maj. J. R. Mackay.
Jackson, Columbia, S. C.....	Lieut. J. M. Birnie, M. R. C.....	Lieut. A. A. Wollin.....	
Lee, Petersburg, Va.....	Capt. Hugh Beebe, M. R. C.....	Lieut. M. B. Chittick.....	Capt. K. A. McClure.
Lewis, American Lake, Wash.....	Capt. N. D. Pontius, M. R. C.....	Lieut. A. Bolenbaugh.....	Lieut. H. Pugh.
Meade, Annapolis Junction, Md.....	Maj. E. S. Linthicum, M. R. C.....	Lieut. E. L. Frederick.....	Capt. G. R. Ralli.
Pike, Little Rock, Ark.....	Capt. A. A. Gassow, M. R. C.....	Lieut. R. A. Baker.....	Lieut. C. P. Isaac.
Sherman, Chillicothe, Ohio.....	Lieut. A. J. Brainard, M. R. C.....	Lieut. J. P. Trickey.....	
Taylor, Louisville, Ky.....	Lieut. L. J. Ifford, M. R. C.....	Lieut. A. H. Waitt.....	Lieut. G. F. Jeanes.
Travis, Fort Sam Houston, Tex.....	Lieut. Daniel Grant, M. R. C.....	Lieut. F. L. Stoonkin.....	Capt. H. A. B. James
Upton, Yaphank, N. Y.....	Lieut. H. W. Snyder, M. R. C.....	Lieut. C. L. Weirich.....	Capt. N. Henton.

NATIONAL GUARD

Camp and location	Divisional gas officer	Chemical adviser	British adviser
Beauregard, Alexandria, La.....	Lieut. F. W. Furman, M. C. R.....	Lieut. V. A. Coulter.....	Lieut. W. D. Seaton.
Bowie, Fort Worth, Tex.....	Lieut. F. B. Gilpin, M. C. R.....	Lieut. R. W. Miller.....	Capt. E. S. Peck.
Cody, Deming, N. Mex.....	Lieut. A. L. Hiekok, M. C. R.....	Lieut. C. N. Austin.....	
Doniphan, Fort Sill, Okla.....	Lieut. Wm. Bane, M. C. R.....	Lieut. Wm. J. Knox, Jr.....	Maj. J. L. Dawson, V. C.
Greene, Charlotte, N. C.....			
Hancock, Augusta, Ga.....	Capt. L. A. Stone, M. C. R.....	Lieut. G. P. Russell.....	Capt. P. Baker.
Kearny, Linda Vista, Calif.....		Lieut. H. S. Bennett.....	Capt. W. H. Lisle.
Logan, Houston, Tex.....	Capt. F. F. Sprague, M. C. R.....	Lieut. W. E. Vawter.....	Lieut. J. L. Therman.
Mills, Garden City, N. Y.....			
MacArthur, Waco, Tex.....	Lieut. C. B. Fair, M. C. R.....	Lieut. R. V. Murphy.....	Capt. A. S. Davy.
McClellan, Anniston, Ala.....	Lieut. G. S. Tillman, M. C. R.....	Lieut. F. O. Amon.....	Capt. G. Murfitt.
Sevier, Greenville, S. C.....	Lieut. Joseph Leidy.....	Lieut. F. B. Sherwood.....	
Shelby, Hattiesburg, Miss.....	Lieut. J. A. Work, M. C. R.....	Lieut. C. E. Howson.....	Capt. V. G. Walsh.
Sheridan, Montgomery, Ala.....	Lieut. O. G. Alexander, M. C. R.....	Lieut. J. H. Bogart.....	Capt. S. Revels.
Wadsworth, Spartanburg.....	Lieut. Lindsay Peters, M. C. R.....	Lieut. O. E. Roberts.....	Capt. H. M. Deans.
Wheeler, Macon, Ga.....	Capt. C. C. Pratt, M. C. R.....	Lieut. R. G. Bailey.....	Lieut. H. E. Plante.

MEDICAL OFFICERS TRAINING CAMPS

Camp and location	Divisional gas officer	Chemical adviser
Fort Riley, Kans.....	Capt. H. C. Parker.....	
Fort Benjamin Harrison, Ind.....	Capt. T. B. Appel.....	
Fort Oglethorpe, Ga.....	Capt. Blase Cole.....	Lieut. H. K. Bear.

INFANTRY SCHOOL OF ARMS

Location	Director divisional gas department	Chemical adviser
Fort Sill, Okla.....	Maj. R. Conard, M. R. C.....	Lieut. E. Y. Titus.

^a Weekly Report, January 5, 1918. Copy on file, Historical Division, S. G. O.

QUIZ COMPEND ON THE USE OF GAS IN WARFARE ^{a,b}

HEADQUARTERS, 79TH DIVISION, N. A.,

GAS DEFENSE SERVICE,

Camp Meade, Md., February 11, 1918.

First and foremost in gas defense is perfect familiarity with the prescribed box respirator and its use. Therefore we place the respirator in the hands of the student for examination and inspection. An explanation of its mechanism is in order.

1. What is the so-called small box respirator?

The so-called small box respirator is the only certain means of defense against toxic gases.

2. How does it function?

It acts as a chemical filter and neutralizing agent to gaseous contaminated air. All inspired air passes through this filter into the mouth and then into the lungs. By passing through this filtering medium the gas-laden air is freed from its poisonous qualities.

3. Of what does it consist?

It consists of the haversack with a sling arrangement (whereby it is carried), a whip cord, and a record card. Inside the haversack, right-hand compartment, the direction card and antidim compound; left-hand compartment, a spring rest and canister. The canister is connected to the trachea tube, the trachea tube to the angle tube, the angle tube to the saliva trap and gill valve, and the latter is connected to the face piece. Inside the facepiece the mouthpiece is connected to the angle tube. The nose clip and two eyepieces are also connected to the facepiece. There are also two elastics and a central tape which hold the facepiece in place.

4. What are its component parts?

Its component parts are the haversack with whip cord, record card, antidim compound, direction card, spring rest, canister, flutter valve, trachea tube, angle tube, gill valve, mouthpiece, nose clips, eyepieces, two elastics, and central tape.

5. Describe the haversack.

The haversack is a canvas bag in which the mask and canister are carried. The edges of the haversack are securely stitched and protects its contents. A ring is securely fastened at the top and each end of the haversack to which a sling is fastened; two buttons or studs on the sling; a leather tab on the left side of the haversack to receive the studs for adjustment from the "carry" to the "alert" position; a flap and two snap fasteners. The haversack is divided into two compartments—the right and left hand compartments. The partition which divides the haversack into two parts has an opening at the bottom which allows the air to pass freely from one compartment to the other. In the right-hand compartment are found the spring rest and canister. In the left-hand compartment the antidim compound, direction card, and the facepiece of the respirator are found. On the right side of the haversack a whipcord is fastened. A record card is attached to the whipcord. The flap, at the opening of the haversack, is buttoned to the front of the haversack at the top.

6. Describe the spring rest.

The spring rest is a heavy wire spring, about 3 inches long and an inch high. It is fastened to the bottom of the right-hand compartment of the haversack. The canister rests on this wire spring, thereby leaving a space between the bottom of the canister and the bottom of the haversack. But for this space, water which may soak through the haversack would settle at the bottom and mix with the chemicals contained in the canister. This space, provided for by the spring rest, allows the air to enter the canister more freely.

7. Describe the record card and explain its use.

The record card is a small white card on the outside of which are strips of adhesive, which are used to repair respirators quickly. This card is attached to the whipcord and is kept clean by being placed in an envelope or pocket. On the record card is written the time the mask was issued; the date the mask, or respirator, was used for drilling purposes; the kind

^a Copy on file, Historical Division, S. G. O.

^b This illustrates what was done in the way of instruction in the home camps when this was under the Medical Department.—Ed.

of attack the mask was subjected to (whether shell or cloud); the length of time the mask was worn; the wearer's name and when and why the respirator was returned. The life of the respirator is about 24 hours.

8. Describe the canister.

The canister is a metal container about 9 inches long and 3 inches wide. A rounded projection is at the top of the canister to which the trachea tube is fastened. At the bottom is a small circular opening, inside of which the flutter valve is fitted. Eight concave ridges, arranged the same distance apart, encircle the inner walls of the canister, into which strips of fine wire gauze are fitted. The wire gauze separates layers of chemicals contained in the canister and also hold the chemicals in place, preventing the chemicals from rattling or moving when the canister is shaken.

9. Describe the flutter valve.

The flutter valve is a small circular disk fitted inside the opening at the bottom of the canister. This disk of rubber rises as you inhale, allowing air to enter the canister. After inhalation the valve drops and covers the opening at the bottom of the canister. The air which has been inhaled into the canister is filtered by the chemicals. The falling of the valve prevents the air from being forced, or escaping, through the bottom, or entrance of the canister.

10. What function does this valve perform?

This valve allows air to enter the canister at the bottom and prevents the air from escaping through the same opening.

11. Describe the trachea tube.

The trachea tube, which carries the purified air from the canister to the mouthpiece, is made of flexible, fabric-covered rubber. It has a circular corrugation, being similar in form to the windpipe of a person; hence the name. Due to its flexibility and corrugated form, it can be turned and moved in any direction without danger of it becoming creased or impaired and thereby shutting out the pure air to the lungs.

12. What should be particularly noted relative to this tube?

The connections of the trachea tube to the top of the canister and the angle tube should be particularly noted. Both connections are tightly wired and then taped so that no air can enter this tube except through the flutter valve in the canister. Care must be taken that there are no holes or breaks in the tube so that no contaminated air can enter.

13. To what does the trachea tube connect?

The trachea tube connects the canister with the mouthpiece by means of the angle tube.

14. Describe the angle tube.

The angle tube, a small metal tube with the form of an obtuse angle, connects the trachea tube and gill valve with the mouthpiece, which is inside the facepiece of the respirator. The tube is so constructed that it contains a saliva trap.

15. Describe the gill valve.

The gill valve is a small sac of rubber with its two lower corners cut off. It is securely fastened to the angle tube by means of wire and also taped. The function of the gill valve is to allow the expired air to escape before it reaches the canister.

16. What is the function of the saliva trap?

The function of the saliva trap is to prevent the saliva from running into the trachea tube which would allow it to pass into the canister, thereby coming in contact with the chemicals, causing their disintegration and shortening their life. Due to this trap, the saliva finds its way out through the gill valve.

17. Describe the mouthpiece.

The mouthpiece, an oval disk of rubber with two projecting tabs, is the upper end of the angle tube inside the facepiece of the respirator, extending upward about 1 inch where it flares out, forming a half circle. The mouthpiece, when inserted in the mouth, the half circle fits between the teeth and the gums and lips. This half circle has inside, pointing inward and upward, two small rubber lugs which are grasped between the teeth; thus the mouthpiece is held firmly in the mouth by the teeth. An opening is provided in the rubber projection where it is fastened to the angle tube which expels the saliva into the saliva trap.

18. How is it placed in the mouth?

To insert mouthpiece, grasp angle tube outside facepiece with the hand, pushing entire mouthpiece into the mouth. Then draw it forward so that the rubber disk fits between the gums and lips, and grip the rubber tube firmly between the teeth.

19. Describe the nose clip.

Just beneath the eyepieces of the facepiece is a small circular wire spring, on the two ends of which are fastened rubber pads. This is the nose clip, and by pinching the spring from the outside these pads are separated, allowing the nose to be placed between them when it is held shut, due to the pressure by these pads.

20. What is its function?

The function of the nose clip is to close the nostrils, preventing the passage of air through them, either by inhalation or exhalation.

21. Why is it necessary to have this nose clip?

It is necessary to have this nose clip to prevent any inhalation through the nose, as the only air which is allowed to enter the lungs must first be purified by passing through the canister of chemicals and then be inhaled through the mouthpiece.

22. Describe the eyepieces.

The eyepieces, the means of vision when the respirator is worn, are two small circular windows of nonbreakable glass securely fastened to the facepiece inside and outside. The fabric is fitted tightly inside by a flat metal ring, and on the outside the metal protrudes enough that the fabric is fastened securely to it by wrapped string. These eyepieces must be tightly fastened to the fabric in order to exclude contaminated atmosphere from inside the facepiece.

23. Describe the facepiece of the mask.

The facepiece of the respirator, which serves to protect the face, is made of a rubberized fabric. The edges are folded in such a manner that we have a seam which lies flat and close fitting against the chin, cheek, and forehead. The stitches of the seams do not come through all layers of the fabric, and therefore no gas can enter the facepiece through them. Fastened to this fabric are two elastic tapes which are held apart at the proper distance by means of a small piece of nonelastic tape known as the metal central retaining tape.

24. What retains same in direct contact with the face?

The facepiece of the respirator is retained in direct contact with the face by means of the two elastics and the central retaining tape.

25. What should be particularly noted about the center head tape?

The central retaining tape should be pulled back smoothly and tightly over the center of the head. This draws the facepiece of the respirator tightly under the chin, causing it to fit close to the cheeks and forehead, thereby preventing the entrance of any gas.

26. How is the fabric of the respirator tested for holes?

To test the fabric of the respirator, hold it up before the light and if there are any pinholes they can be seen, due to the light shining through.

27. How is the flutter valve tested?

The flutter valve is tested by holding the gill valve between the first and second fingers of the hand and exhaling through the mouthpiece. If the valve is working properly no air can be exhaled.

28. Why is it necessary to test this valve?

It is necessary to test this valve, as it is through this valve that the air must enter the canister and also when it closes it prevents the exhaled air from passing through the canister, but forces it out through the gill valve.

29. How is the respirator tested for tight connections?

The respirator is tested for tight connections by a careful inspection of the various parts. This examination is verified by the following test: Close gill valve between the fingers and exhale through the mouthpiece, and if all connections are tight no air will escape.

30. How would loose connections interfere with the proper functions of the respirator?

Loose connections would interfere with the respirator by permitting gas-contaminated atmosphere to be breathed into the lungs without it passing through the canister first.

31. Would this be dangerous to life in a gas-contaminated atmosphere?

This would be very dangerous indeed to live in a gas-contaminated atmosphere.

32. What is particularly noted about the stitching of the fabric of the facepiece?

It should be particularly noted that the stitching of the fabric of the facepiece is secure and that no holes are produced by it inside the facepiece. This is accomplished by having the stitches covered over by strips of the fabric being cemented over them, and this strip should be tightly held in its proper place.

33. What should the haversack contain besides the respirator and its component parts? The haversack should contain nothing else.

34. How are the eyepieces prevented from fogging?

The eyepieces are prevented from "fogging" by using the antidim compound. This compound is impervious to water or moisture. A thin film of this is placed on the inside of each eyepiece before the respirator is used.

35. How is the facepiece of the respirator cleaned, or cleared?

The facepiece is cleared of any gas which may have entered during the adjustment of the respirator by taking a deep breath, removing the mouthpiece and blowing into the facepiece, thereby ballooning it from the face. The mouthpiece is replaced and the facepiece pressed tightly against the face by the hands, which causes the contaminated atmosphere to be forced out at the sides. This is repeated several times and serves effectively to remove any poisonous gases which may have been in the facepiece.

36. How is the respirator worn in the carry position?

In the "carry" position, the respirator is worn suspended with the sling across the right shoulder, and the haversack resting against the left hip with clasped edge of flap next to the body.

37. How do you change from the "carry" to the "gas alert" position?

Pass the left arm backward and between the body and the sling, and by a twist of the body swing the haversack to a directly in front of the body position. With both hands open clasps on flap of haversack. Take leather tab (on upper left-hand corner of haversack) with right hand and raise the sack to a position in front of chest. At the same time clasp the buttons high up on the sling with the left hand. Engage the tab and button. Take whipcord from haversack, pass through the small ring on the right side of haversack, pass whipcord around body and through ring on left side of haversack and tie securely with "slip knot." Carefully close the flap on haversack to protect respirator from weather. Do not fasten the clasps on flap.

38. What are the two ways of adjusting the haversack in the "alert" position?

The haversack may be adjusted in the "alert" position, as described in No. 37, or as follows: Instead of engaging the leather tab and the button, raise the haversack to the position in front of the wearer's back. Pass the whipcord around the body and through the sling thus adjusted. Tie the whipcord as above.

39. Are they both practical at all times, and what advantages has one over the other?

The second method of adjusting the haversack is not practical when troops are wearing full equipment and heavy packs. When practicable, the second method has the advantage of relieving the "drag" upon the wearer's neck and is more comfortable for long periods of wear.

40. Enumerate the three positions for the respirator in zone of operation.

The three positions for the respirator in the zone of operations are as follows:

(a) The "alert" position.

(b) The "carry" position.

(c) The position which is regulated only in so far as the respirator must be near by, within easy reach of the owner, at all times.

41. At what points in the battle line are these positions authorized?

(a) Within 2 miles of the front line all respirators must be worn in the "alert" position.

(b) In the area between the 2 and 5 mile lines the respirator is worn in the "carry" position.

(c) In the area between the 5 and 12 mile lines the respirator may or may not be on the body, but must at all times be within easy reach of the owner.

42. Give the formation for the inspection of masks.

Each man removes the respirator from the haversack which is worn at the "alert." The canister is held under the left arm and the left forearm is extended, facepiece of the respirator held in the left hand, angle tube in the palm of the hand, with the facepiece opened. When this position has been assumed stand at attention.

43. How often is this resorted to in France?

Standing orders in France require that at least one inspection of respirator be made by an officer each day. In many cases a second inspection by either the officer or the gas non-commissioned officer is required.

44. Why is respirator inspected?

Inspections are resorted to chiefly for the purpose of determining whether the men are individually inspecting their own respirators. Each man is made directly responsible for the condition of his respirator, and any man found negligent is severely punished. When a man discovers any imperfection or defect in his respirator he must report the same without delay to the gas officer.

45. What takes place preparatory to mask drill "by the numbers."

Preparatory to mask drill, the men are placed in the following formation: Form two sides of a square, with men in single rank and facing toward the inside of the square. The instructor takes position in the center of the square facing his men. Formation is best assumed by having them "fall in" in double rank facing the instructor. Give the following commands: "Rear rank, left face; column right; march." "Rear rank, halt." "Rear rank, right face."

46. What would you gain by having mask drill "by the numbers."

The chief element sought in mask drill by the numbers is "form." Correct form comes only with continuous practice, and in antigas training we strive to make the donning of the respirator a matter of second nature among the men. Frequent drills "by the numbers" will cause the donning of the respirator in the prescribed form to become almost automatic on the part of the men so trained.

47. What action takes place in No. 17.

With both hands open haversack by pulling the flap forward. Insert the right hand and grasp the facepiece of the respirator, holding the angle tube in the palm of the hand.

48. What action on No. 2?

Mask drill by the numbers, No. 2. Remove mask from sack and seize it with both hands. Grip the edge of the mask by the fingers with the thumbs pointing upward and inward under the elastics. Lean body forward and throw chin well forward.

49. What action on No. 3?

Dig the chin well into the mask and at the same time draw the elastics over the head as far as they will go, until the central retaining tape is stretched taut.

50. Give No. 4 of the mask drill by the numbers.

With the right hand seize the metal angle tube outside the facepiece and push the rubber mouthpiece well into the mouth. Draw mouthpiece forward so that rubber flange is between the lips and the teeth. Grip the two small rubber projections with the teeth.

51. Give No. 5 of the mask drill by the numbers.

Open the nose clip by pinching from the outside the circular wire spring below the goggles; push the slip pads on the lower part of the nose, and release spring. See that the nostrils are completely closed.

52. Give No. 6 of the mask drill by the numbers.

Make general adjustment. Smooth around the edges. See that the mask fits snugly around the jaws and forehead.

53. What do you always do after having the mask completely adjusted, without orders?

(a) Clear the mask of any gas that may have found lodgment within the facepiece during adjustment.

(b) Clean the eyepieces, which will have become "fogged."

54. How are the respirators cleared?

Take a deep breath through the mouthpiece; remove mouthpiece and exhale into face of respirator. Replace mouthpiece. By pressing with the hands on the outside of the respirator, force the air out under the edges of the respirator. If mask fits very tightly lift the edge of the facepiece and force air out. Repeat operation at least three times.

55. How are the eyepieces cleaned?

If the eyepieces become dull they are cleaned by inserting one or two fingers (on the outside of the mask) into the pockets of the fabric alongside the goggles and wiping the inside of the glasses. The eyepiece is held between the thumb and forefinger of the other hand while this is being done.

56. What is the standard adjustment test?

Donning the respirator from the "alert" position in six seconds is known as the standard adjustment test. This does not include the general adjustment cited under No. 6 in mask drill by the numbers.

57. What conclusions and lessons may be drawn from the British attack on the First Naval Brigade at Nieuport, in so far as training goes?

(a) Men near front lines must be constantly on the alert and prepared for gas attacks regardless of seemingly unfavorable weather conditions. (The Germans thought that their nearness to the sea was protection against attack, and on this particular day considered an attack impossible because of the high velocity of wind.)

(b) Men must be carefully trained before joining their units at the front. (In this case, the Germans had every reason to expect an attack after they had raided the British trenches on October 2 and discovered the preparations that were being made, yet on October 5, when the gas was sent over, their men were found to be inadequately trained and heavy casualties resulted.)

(c) In general, it may be said that discipline, constant vigilance, and proficiency in the use of the respirator are the only means of safeguarding your lines against this weapon of warfare.

58. Tell something about the necessity for protection and the enormous casualties resulting from the use of gas. Also give some statistics relative to the return of wounded from the ordinary weapons of warfare as compared with gas.

The Medical Corps are making remarkable progress in their work of returning non-effectives to the lines as effectives. In a large proportion of cases, a man wounded by shell or bullet can be returned to the front. The Germans early in the war returned 69 per cent of all wounded; the French returned 24 per cent. Later the French raised the percentage to 69 per cent, while the Germans succeeded in raising their figures to the astounding mark of 91 per cent. At present the Germans are able to return approximately 89 per cent, and this percentage is slowly decreasing as men are being sent back to hospitals after being wounded numerous times and their vitality correspondingly sapped. The English are returning about 87 per cent. Men who have been gassed seldom return. They are of practically no use to the army, and in a majority of the cases are of no use in a civil community. So pronounced is the effect of the poisonous gases used in warfare that there is practically no hope of returning them to the line. Hence, we must rely almost entirely upon the principles of prevention. It is to teach the principles and methods of prevention that this course has been instituted.

59. Give a brief outline of the use of gas in warfare.^c

* * * * *

On April 22, 1915, the Germans sent dense clouds of chlorine against the unprepared British forces at Ypres. The British (principally Canadians) suffered enormous casualties, and only their ignorance of real conditions in the British lines prevented the Germans from breaking through to Calais. Four days later the Germans let out a similar attack against two French battalions who were making an attack on the German lines. The attack was quickly and completely broken up by the gas clouds. Within a few months gas shells made their appearance in continually increasing numbers, cloud attacks became numerous, both sides took up the new method, and gas became one of the recognized weapons in warfare.

60. Briefly outline the development of the respirator to its present stage of perfection.

The first masks consisted of patches of gauze saturated in sodium bicarbonate and sodium thiosulphate solution. Later, the black veil mask was used in conjunction with goggles, which protected the eyes against gas. Then came the baglike helmets which completely covered the head. These were saturated with phenolate and were called P helmets. Then hexamine was added to the solution to protect against phosgene, and the helmet was then known as the P H helmet. The goggles had given place to eyepieces in the helmet itself, and these eyepieces were further improved. Then came the box respirator developed from an apparatus produced as a filter for gas-contaminated atmosphere. This box respirator has been improved from time to time and is now used by England, America, and France.

61. Enumerate the various kinds of gas according to their effects upon the human economy.

- (a) Lacrymatory.
- (b) Asphyxiating.
- (c) Suffocating.
- (d) Paralyzant.
- (e) Skin irritant.

^c A brief outline of the earliest recorded use of gas in warfare omitted.

62. What effects do they produce and how is the man rendered unfit to hold his place in the fighting line?

(a) Lacrymatory gases cause intense inflammation of eyes and temporary inability to see.

(b) Asphyxiating gases affect the mucous linings of the breathing apparatus and thereby prevent air cells in lungs from taking up oxygen. In addition to immediate effects, secondary effects will develop and more or less permanently impair the lungs and breathing apparatus of any man who survives attack.

(c) Suffocating gases cause death by spasm of the glottis, completely stopping all entry of air into trachea tube and lungs.

(d) Paralyzant gases cause death by paralysis of the central nervous system.

(e) Skin irritants cause erosive burns of the skin. They cause death if the burns cover one-third of the surface of the body (first degree burns).

63. Enumerate the various ways of producing a gas attack.

(1) Cloud; (2) shell; (3) projector; (4) emanation.

64. Describe in detail how these methods are used effectively.

(a) *Cloud method*.—Bury cylinders of liquid gas under fire steps of front-line trench. Connect groups of cylinders to lead outlet pipe with nozzle in front of trench. When conditions are favorable open tank outlets and gas rushes through pipe and forms cloud in front of outlet nozzle. The gas must be heavier than air and the cloud will be forced by the wind to the enemy trench. Hence, wind must be in a favorable direction and of such velocity that cloud will not be scattered before it reaches enemy line. A 3 to 15 mile per hour wind is most favorable. In this method we secure a strong concentration covering large area.

(b) *Shell method*.—Shells containing liquid gas and small charge of explosives are thrown into enemy lines. Shells burst and liberate small clouds of gas. This method is economical, requires little preparation, allows for surprise, and can be used effectively for counterbattery and barrage work. Shells may be dropped at any point within range.

(c) *Projector method*.—Consists of hurling large cylinders of liquid gas into enemy lines by means of improvised mortars. Cylinders burst in enemy line, thus insuring strongest concentration of gas at desired point. Allows for the element of surprise.

(d) *Emanation method*.—A possibility which has not been utilized consists of "planting" in a trench, about to be vacated, some chemicals which will give off toxic gas when the enemy occupies trench.

65. What method has the greatest military value and why?

The projector method has the greatest military value because it embodies all advantages of the cloud and shell attack; i. e., it allows for heavy concentration over large area and for the element of surprise. In addition, the method is economical, easily prepared, and results in the heaviest concentration at the desired point.

66. What properties must a gas possess to render it of service in warfare?

(a) Density. It must be heavier than air.

(b) Diffusion. Must be heavy so that it will diffuse away slowly.

(c) Toxicity. Must put a man out of action either permanently or temporarily.

(d) Vapor pressure. If chemical substance used in shell is a liquid it must give off enough vapor to produce the desired result.

(e) Liquefiable. Gas must be easily and safely liquefied.

(f) Availability. Gas must be obtainable in large quantities since tons of material are necessary for successful attack.

67. What conditions predispose to a successful attack?

(a) A wind blowing steadily in the direction of the enemy with a velocity of 3 to 15 miles per hour.

(b) There should be no rain, but should have moderate temperature and darkness. Fog serves to hid coming cloud and is considered an advantage.

In shell attack, weather conditions are of less importance, but wind should be moderate. A dead calm is also favorable since the gas is liberated at the desired point.

68. What caliber guns are gas shells used in?

Gas shells may be fired from all calibers of guns. The Germans use chiefly the Minenwerfer gun (5.9). The French use chiefly the 75's. The English use the 6-inch howitzers and some of their larger pieces.

69. Describe the different types of gas shells.

Gas shells may contain gas and high explosives, in which case a heavy plate is inserted between the gas and the charge to prevent the body of the shell from being shattered with too much force. Too violent explosion serves to scatter the gas and render the gas less effective. The ordinary shell contains a low-explosive charge which serves to lay the shell open and spray the gas over a limited area. Gas shells are made with blunt head, explode on contact, and are of all calibers. Any form of gas may be used in shells.

70. How are gas activities detected?

Preparations for gas cloud attacks are usually detected prior to the development of the attack. Listening posts should detect the unusual noises incident to burning cylinders. Observation posts may detect undue activities in enemy lines. Airplane observations frequently warn of attack. Raiding parties, sent out to determine meaning of unusual noises, should bring in desired information. Finally, sentries may learn of attack and must detect the coming cloud by its smell before it hits the men in your line.

71. What are the positive signs of a gas cloud attack?

1. The hissing sound resulting from the escape of gas through outlet nozzles.
2. Appearance of cloud over enemy line.
3. Odor of gas.

4. For the halogen gases the tobacco test is positive. Tobacco smoke loses its flavor in presence of these gases.

72. How are gas shells distinguished from ordinary shells?

- (1) By a wabbling noise as shell comes through the air instead of a steady whine.
- (2) By a dull thud as shell strikes ground instead of high, loud explosion.
- (3) By puff of white smoke after the shell explodes.
- (4) By the marking on shell or on fragments of the shell.
- (5) By ogival shape of nose of shell instead of sharp, armor-piercing point.

73. What is the tobacco reaction?

Tobacco, when smoked in atmosphere containing gas, is said to lose its taste and the smoker loses his desire to smoke.

74. How are warnings conveyed in gas-cloud attacks?

In gas-cloud attacks, the warning must be general and is conveyed mainly by use of the strombos horns, also by beating on bells, sections of rails, steel triangles, and empty shell cases, and any instrument which will make a noise and does not require the use of a man's lungs.

75. Describe the strombos horn.

A strombos horn is an instrument blown by a small cylinder of compressed air joined to the horn proper by a heavy rubber tubing several feet long. The horn has a megaphone attachment from a small circular box where the air causes a circular metal disk to vibrate, giving off the sound. An extra cylinder of air is included in the apparatus and the whole is packed in a strong wooden box.

76. How are these horns operated? By whom and how are they arranged to convey the necessary warning?

These horns are operated by releasing the compressed air from a cylinder by means of a stopcock opened by hand or foot pedal. A sentry stands at each, ready to sound the horn when he smells or detects the presence of gas. They are arranged by the officer in command of a sector so that there is one to every 400 yards along the front and another parallel row every 600 yards in rear. The horns of one row back of the interval of the row in front, checkerboard fashion.

77. What means of determining when wind and weather conditions predispose to an attack are used in the front-line trenches?

A simple wind vane and Beaufort flag, together with the observation of certain material objects, are used to determine wind and weather conditions in the front-line trenches. The Beaufort flag and natural objects are observed and results referred to the Beaufort scale which translates their behavior into velocity of the wind per hour.

78. What is a wind report? Who is charged with making same and where is it sent?

A wind report is a record of the results of the observations of weather condition made at prescribed intervals by the company gas officer's assistant, the company gas noncommissioned officer, and frequently (several times daily) sent to the division gas officer through military channels.

79. Prepare a typical wind report.

Trench No. 67.

JAN. 27, 1918.

Time	Direction	Velocity	Remarks	Signature
A. m. 6.00---	W.	2	Variable-----	T. S. D.
9.00---	W.	5	Variable-----	T. S. D.
Noon 12.00---	WNW.	5	Variable-----	T. S. D.
P. m. 3.00---	WNW.	10	Steady-----	T. S. D.
6.00---	WNW.	10	Shifting-----	T. S. D.
9.00---	N.	10	Steady-----	T. S. D.
9.30---	N.	10	Shifting-----	T. S. D.
10.00---	NNE.	5	Variable-----	T. S. D.
10.30---	NNW.	2	Variable and shifting-----	T. S. D.
12.00---	W.	5	Variable-----	T. S. D.

80. What scale is used in determining wind velocity?

The Beaufort scale is used in determining wind velocity.

81. Give this scale.

Beaufort scale

No.	M. P. H.	Observation of natural objects	Behavior of flag
0	0	Smoke goes straight up-----	No movement.
1	2	Smoke slants-----	No movement.
2	5	Wind felt in face-----	Slight movement.
3	10	Paper moves on ground-----	$\frac{3}{4}$ way up.
4	15	Small bushes sway-----	Up and falling.
5	20	Tree tops sway and water ripples up-----	Falling less often.
6	30	Waves on water-----	Up and flapping.

82. How often are these reports and observations made?

These reports are made at least every three hours if the wind is not from a dangerous direction, more often if near or approaching a dangerous direction, and every half hour if from a dangerous direction.

83. What precautions are necessary in setting up a weather vane?

Precautions necessary in setting up a wind vane are:

- (1) That it is not observed by the enemy.
- (2) That it be set high enough where an unobstructed wind can reach it.
- (3) That it be set level and the supports oriented (north and south).
- (4) That it be set in a representative section of the trench.

84. Describe in detail the ordinary vane and attached Beaufort flag used on a company front.

An ordinary weather vane has two horizontal light sticks about a foot and a half long crossed at right angles at their middles with a similar vertical stick rising about 18 inches from their intersection. This supports a light wire or wooden beam, balanced on a pivot, so that it can be swung in a horizontal plane by the force of the wind on a thin flat rudder on one end of the beam. The rudder must have an area of 5 or 6 square inches so that it will be swung in the direction of the wind and cause the beam to point directly into the wind. On a continuation of the upright and about 8 inches above the beam the Beaufort flag is attached. It is a triangular piece of bunting 5 inches long and three-fourths inch wide. The wide end is attached to the upright by a very short string.

85. Enumerate the several points of the mariner's compass as used in determining direction.

See chart in answer to question No. 79, sheet No. 11.

86. What velocity of wind do the Germans prefer in making a gas attack?

The Germans prefer an 8-miles-per-hour wind in making gas-cloud attacks.

87. What precautions should be taken when an attack is probable and the wind is in a dangerous direction?

When the wind is from a dangerous direction and an attack is probable, the following precautions are taken in addition to usual precautions:

- (1) Wind observations are made every half hour.
- (2) Frequent inspections are made of respirators, sentries for gas alarms, alarm devices, antigas trench stores, dugout entrances where gas-proof blankets are to be let down, and signals for warning artillery and for calling artillery support.
- (3) Men sleep on fire step.

88. Enumerate and describe all the alarm devices used to sound warnings for attack by shell or cloud.

Bells (any ordinary loud bell).

Steel rails (straight or triangular, with only one point of support so they may vibrate when struck).

Empty shell cases (metal cylinder similar to bell).

Rattles (notched wheel turning with a handle causing a flat wooden strip to vibrate when turned against it).

For gas cloud: Same devices with the addition of the strombos horn (described above, answer No. 75).

The telephone and buzzer are also used to warn troops in rear.

89. What precautions should be taken relative to sentries at night?

At night, sentries on the lookout for gas should have near them one man awake but resting and one man asleep who relieves the others every hour. They should have something (for example, buckets of water) to kick into dugouts to awaken men there while the sentry proceeded to put on his own mask with his hands. The sentry should have nothing to impede his sight or hearing.

90. When should men sleep on the fire step rather than in the provided dugouts?

Any men who sleep in any of the forward trenches at any time should do so on the fire step rather than in dugouts so that they may be easily roused in case of gas attack and be less liable to gas, due to their raised position.

91. What action should be taken in the trenches upon a gas alarm?

(1) All men should be roused and should put on their respirators, holding their breath until adjustment is effected.

(2) All officers, artillery, regimental and other headquarters, and troops in rear should be warned at once.

(3) All men to stand at arms where the situation demands (troops in gas firing slowly; flanking troops ready to pour a heavy fire on any advancing enemy).

(4) All blankets at gas-proof dugouts are let down and kept wet.

(5) All movement and unnecessary noise and talking ceases.

(6) The gas noncommissioned officers report at once to their company gas officers.

(7) The company commander calls for artillery support by prearranged signal.

92. What action does the artillery supports take upon the liberation of any enemy gas cloud?

The supporting artillery pours a heavy fire on the trenches where the gas is being liberated and the trenches in rear, and also puts down a light barrage in No Man's Land to scatter the gas as much as possible.

93. By what means are dugouts and bombproofs protected from the entrance of gas-contaminated air?

Dugouts and bombproofs are protected from the gas-contaminated air by gas-proof blanket doors.

94. Describe in detail this construction.

Two frames are made to fit the passage to the dugout or bombproof of planed boards strapped with strips of blanket. The outer one leans toward the chamber and the inner one way from the chamber. These are set about a yard apart in the entrance. A blanket is hung over each so that when let down it will completely close each frame and form a small chamber between the frames. Light laths may be tacked to the blankets to make them fit the flat surfaces of the frames. These blankets are kept rolled up at the top of the frames and kept wet so that they will seal with the frames when let down and prevent gas reaching the dugout, the double door allowing a man to enter without bringing much gas into the shelter with him.

95. When is troop movement to stop during a gas attack?

Movement of troops is to stop during a gas attack if it is at all compatible with military necessity.

96. What action is to be taken in billets and in the rear areas during a cloud attack?

Troops in billets and rear areas during a gas-cloud attack are at once roused and put on respirators immediately the gas is apparent, let down blankets protecting cellars, etc., and keep these blankets wet. All movement ceased other than that which is of military necessity.

97. When is the most favorable time, wind and weather conditions being right, to launch a gas attack?

The most favorable time to release a gas attack (wind and weather conditions being favorable) is when a relief is in progress in the enemy trenches, crowding the trenches with men and equipment, especially if this relief is at night (always a good time for gas).

98. Who gives the command to remove respirators?

The company commander gives the command to remove respirators.

99. When is the command given, and how long after the attack?

When the trenches, etc., have been cleared of gas after the attack, and pronounced clear of gas, a half hour is allowed for safety, and then the command to remove respirators is given.

100. How are orders given when the gas respirator is being worn?

To give an order while wearing the respirator, take a long, deep breath through the mouthpiece, remove it from the mouth, give the command on this breath, replacing mouthpiece before another breath is taken. If command is too long for one breath, break it up into parts which can be given on one breath.

101. Who is responsible for taking over antigas trench stores, and when should this be performed? Give reasons.

The company gas officer is responsible through his gas noncommissioned officer for taking over the antigas trench stores when relieving a trench. This should be performed in the daytime previous to the actual relief, so that the stores may be properly inspected and their position made familiar to the gas noncommissioned officer in case they would be needed soon after his company comes in.

102. What duties are concerned preceding a gas attack?

Before an attack the company gas officer, assisted by the company gas noncommissioned officer, supervises the antigas training of the men in the company.

(1) Takes over the following trench stores:

- (a) Strombos horns and other alarm devices.
- (b) Antigas fans and fuel.
- (c) Vermorel sprayer and antigas solution.
- (d) Gas-sampling apparatus.
- (e) Wind-observation apparatus.

(2) Takes the following precautions:

- (a) Daily inspection of respirators, alarms, and trench stores.
- (b) Respirators worn in "alert" within 2 miles of front, "carry" within 2-5 mile zone, near at hand within 5-12 mile zone.
- (c) Inspects sentries posted at alarms, dugouts, headquarters, and with each separate body of men (each has one man watching for gas) as to position and knowledge of duties.
- (d) Men sleep on fire step in forward trenches. At night each sentry has two men to spread the alarms.
- (e) Dugouts properly made with well-fitting wet curtains, properly rolled up.
- (f) Wind observations properly made.

103. What action takes place in the trenches during an attack?

Sound alarms and all men stand to arms. Send back "gas" to division headquarters, who order an 18-pound barrage on No Man's Land. Flanking troops get ready to fire. If the infantry attack follows, the S O S is sent which calls for heavy bombardment from all available guns and flanking troops.

104. What duty especially concerns the gas noncommissioned officer during an attack?

During a gas attack the gas noncommissioned officer records every observation concerning the conditions of the attack which he can make, and collects samples of the gas, shells-water, and ground which contain gas, times the attack, and includes all this in a report to the company gas officer.

105. Shelters, dugouts, and bombproofs after an attack are protected by what methods?

Shelters, dugouts, and bombproofs are freed from gas after an attack by ventilation, fires, fans, or spraying with antigas solution in Vermorel sprayer.

106. Describe these various methods in detail considering shelters of all kinds.

All ventilators and entrances are opened to allow the circulating air to take out the gas; fires of split wood and coal oil are started where they will cause the best circulation of air

and allowed to burn on a small brazier for 5 or 10 minutes (1 pound of split wood to each 200 cubic feet of space). If no fuel is available, fans (Ayrton fans, sacks, etc.) are flapped to cause the draft. The spray is now only used to spray beneath floors or on floors where gas may be hidden. In a compartment with only one short opening the fire can be near the center of the compartment; if the opening is long the fire will have to be put near its inner end. If there are two openings the fire can be made in the inner end of one opening.

107. Describe the antigas fan.

The Ayrton fan consists of a canvas fanning surface mounted on a frame attached to a short, light, straight wooden handle (2 feet long). The fanning surface is stiff in the center—due to the frame edges—with the edges more pliable; these loose when fan not in use over the stiff center to form folding a compact square. When open the fanning surface is 24 inches long and 16 inches wide. It is 8 inches square when folded.

108. How long after a shelter has been cleared is it safe to occupy same without respirator? (Presuming both asphyxiating and lacrymatory gases have been used.)

Dugouts and other shelters should not be entered without respirator until four hours after clearing.

109. When clearing a dugout by fire, how long should the fire be kept burning?

The fire should be kept burning for at least 10 minutes. Tests for gas should be made from time to time.

110. What is used for these fires, and what amount do you count upon doing efficient work?

The best fuel is dry wood, finely split, with a little kerosene (paraffin) for lighting purposes. One pound of wood will ordinarily clear of gas 200 cubic feet of air space.

111. How is the material kept and where?

This material is kept in a covered tin can in the dugout in which it is to be used.

112. What is a Vermorel sprayer?

A Vermorel spray is very much like the ordinary small tank (3-gallon) tree sprayer (the type which one can carry and operate).

113. What is its use?

It is used for keeping the blankets wet at the entrance of a gas-proof dugout. It may be used to spray the floor of a dugout after clearing with fans or fire. The alkaline solution used in it neutralizes any gas that may remain in the dugout.

114. What is the solution used therein?

The solution used in the Vermorel spray is as follows:

3 gallons water (one large bucket).

1½ pounds sodium thiosulphate (hypo).

3 pounds sodium carbonate (washing soda).

115. Where and how is it kept?

This solution is kept in corked demijohns or other closed vessels near the sprayer.

116. How many Vermorel sprayers are used or issued per company?

Sprayers are used on a basis of two per company.

117. How are shell holes treated?

Shell holes should be covered with at least 18 inches of earth, and all places around the hole where the liquid contents of the shell has spilled should be covered. The place should be marked, and should not be disturbed.

118. What disposition is made of blind shells?

"Blind shells" (i. e., shells which fail to burst) should be investigated, made safe, and sent back to the division gas officer along with the report of the attack.

119. What effect does gas have upon arms and ammunition?

Gas has a very injurious effect upon arms and ammunition. It rapidly corrodes and destroys exposed metal parts.

120. How are they protected from this effect?

Oil cleaning will prevent corrosion for about 12 hours. The first opportunity should be taken to dismantle the arms and clean the parts in boiling water containing a little washing soda (a teaspoonful to a quart of water). If this is not done corrosion continues slowly even after oil cleaning, and may render the arms useless. Ammunition should be cleaned and oiled after an attack and expended as soon as possible.

121. How are small arms cleaned after a gas attack?

Small arms are usually cleaned by taking the arms down and boiling or washing the parts in the soda solution.

122. What is done with the machine-gun cartridge belts, grenades, etc.?

Ammunition in machine-gun belts exposed to gas should be replaced by fresh ammunition, and after cleaning should be used by riflemen as soon as possible. Grenades should have safety pins and all working parts cleaned and reoiled.

123. Is food affected by gas?

Food may be contaminated by gas, and after being exposed to gas should be destroyed. Food in gas-proof containers would not be affected.

124. How are mortars and big guns protected?

All bright parts of mortars and big guns should be kept coated with oil and kept covered when not in use.

125. How are range finders and sights protected and cleaned?

Sights and all instruments should be smeared with oil, and protected with covers. Be careful that oil does not come in contact with any lens or get into the interior of the instrument.

126. How are instruments of precision, such as telephones, switchboards, electrical devices, and buzzers protected and cleaned?

Such instruments can only be fully protected by keeping them in dry gas-proof dugouts. As much as is consistent with proper use, they should be kept in leather cases or covered with cloths or blankets. After a gas attack, terminals and exposed metal parts should be scraped, cleaned with a cloth dampened in a soda solution, and then dried. If the internal portions of the instrument have suffered, it should be sent back to the rear to an instrument repairer.

127. Why is it necessary that line men should know something about the emergency treatment of gas cases?

Because in the field, and especially in the trenches, the Medical Department is frequently not available, and men of the line must give first aid.

128. How are toxic gases classified in so far as the emergency treatment goes?

(1) Irritants to lungs and breathing apparatus, generally.

(2) Eye irritants.

(3) Those which prevent the blood from taking oxygen.

(4) Poisons to the central nervous system.

(5) Skin irritants.

129. Give the emergency treatment of one overcome by the first group.

Move the patient out of gas. Separate severe from light cases. Watch for possible collapse. In case of collapse, or if patient has difficulty in breathing, give inhalations of ammonia, and give internally 15 to 60 drops of aromatic spirits of ammonia in water. Remove tight clothing and equipment. Evacuate lying down. Do not let patient walk or exert himself.

130. Give the emergency treatment of one overcome by the second group.

Place patient in dark dugout if possible. Apply wet compress to eyes (first-aid packet must not be used for this). Eye lotion made of equal parts of witch hazel and saturated solution of boracic acid should, if possible, be dropped in eyes.

131. By the third group.

Get patient out of gas. Use artificial respiration (Sylvester method). Stimulate with coffee or brandy. Douse head and chest with cold water. Elevate feet and lower head. Induce vomiting. Keep warm.

132. By the fourth group.

Dash cold water in face. Break ampules of ammonia and hold under nose. There is little to be done here but get victim in fresh air.

133. By the fifth group.

Remove clothing which may have absorbed liquid from shell and apply wet compress of solution, used in Vermorel spray, 1 part to 8 of water, to burn. Use first-aid packet here.

134. What concentration is chlorine fatal in at once?

One part of chlorine to 10,000 parts of air.

135. What concentration is hydrocyanic acid fatal in?

One part of hydrocyanic acid to 100,000 parts of air.

136. What concentration is phosgene fatal in at once?

One part of phosgene to 25,000 parts of air.

137. Is there any record in which men have been gassed in lesser concentrations?

Men have been "gassed" by sleeping in blankets which have been exposed to gas.

138. What danger is particularly present in so far as gas is concerned in billeting in France?

Most of the billets in France are heated by charcoal braziers. As there are no chimneys or flues attached to these braziers, the products of combustion remain in the room. If ventilation is poor, the supply of oxygen is insufficient for complete combustion of the charcoal, and a very insidious and deadly gas, carbon monoxide, is formed. This gas is fatal if more than 0.5 per cent is present in the air. The small box respirator is no protection against this gas.

139. What symptoms would a man suffer from poisonous doses of the different classes of gas already mentioned?

Symptoms of poisoning by a lung irritant are that victim feels suffocated, coughs, and may become blue from lack of air. There is great discomfort and pain in the chest. Victim tears at clothing, and after a time collapses and succumbs to heart failure. Some of the lung irritants have delayed action and do not cause much irritation or inconvenience immediately. Some hours after exposure to the gas the victim will collapse. Symptoms of lacrymatory or tear-producing gases are a profuse flow of tears, acute inflammation and swelling of the lining of the eyelid, and finally total inability to see. Gases which prevent blood from taking up oxygen are insidious in their action, and produce a sense of weakness in the limbs. Victim may become excited, and shout, laugh, and sing like a drunken person. There may be violent headache. Apathy and complete helplessness follows and death soon ensues.

Symptoms of poisoning by gases which act on central nervous system are vertigo and confusion, headache, blurring of vision, palpitation, pain over heart, and labored breathing. In a fatal dose there is immediate unconsciousness, dilatation of pupils, gasping respiration, and death, with or without convulsions. Symptoms of skin irritants would be inflammation and erosion of the skin, blistering, and swelling. The portion of the body covered by the clothing suffers most.

140. Are the effects of a lacrymatory gas permanent? If not, how does it possess military value?

The effects of a lacrymatory gas upon the eyes are not permanent. The inability to see lasts only a short time. Its military value is due to the fact that it temporarily disables its victims and puts them out of action.

141. How can carbon monoxide be detected or suspected if it has no odor, color, taste, and is nonirritant?

Carbon monoxide may be detected by its effects upon birds or animals exposed to it. A fraction of the percentage required to kill human beings is fatal to canary birds and mice.

142. If it possesses all these properties besides being toxic, why is it not used intentionally in warfare?

It is not used intentionally in warfare because the only protection against it as yet devised is the oxygen-tank apparatus. The small box respirator is of no value here. Hence it would be impossible to follow the gas attack with an infantry attack. The wind might shift and carry the gas back over the persons liberating it. It is not advisable to use a gas that your own respirators or mask will not neutralize.

143. Why does not the respirator authorized and used by our own forces handle the carbon monoxide gas?

This gas has an affinity for the hemoglobin of the blood 210 times greater than oxygen or air. It replaces the oxygen necessary to carry on metabolism or life. There is no chemical substance known that will filter or neutralize this gas. It is necessary to utilize an apparatus which will supply the necessary oxygen.

144. What is the specific gravity or weight of hydrocyanic acid? Also chlorine?

Specific gravity of HCN, 0.96; specific gravity of Cl_2 , 2.46.

145. Could hydrocyanic acid be used in cloud attack? If not, why?

No. It is lighter than air, hence would not stay close to the ground.

146. Give the Sylvester method of artificial respiration.

Place patient on back; put something under small of back to expand chest. Push patient's hands in under ribs with pressure and draw them out sideways until over head. Repeat 16 to 18 times a minute. Keep tongue from falling back in throat by pin or handkerchief, etc.

147. Give a brief summary of the organization of our antigas service.

The antigas service, which is in the hands of the Medical Corps, is divided into four branches, as follows: Field supply, which has to do with the manufacture of all respirators and furnishing of supplies; overseas repair, which has to do with keeping the respirators in repair behind the lines in France; field training, which has to do with the training of all the men, in the use of the respirators and antigas measures; chemical branch, which has charge of research work along chemical lines pertaining to gas warfare.

148. Enumerate the duties of a company gas noncommissioned officer.

DUTIES BEFORE ATTACK

Assists gas officer in supervision of training of men for gas defense. Takes over stores (gas defense) in trench during afternoon of day unit is to go into trenches.

Inspects masks and alarms daily.

Sees that masks are worn at "alert" 2 miles from front line

Sees that sentries know their duties and are familiar with use of Strombos horns.

Sees that all gas-defense appliances are in working order.

Wind observations are taken regularly.

DURING AN ATTACK

Reports to gas officer immediately.

Sees that all men don their masks and that sleeping men are aroused.

Artillery is notified.

Blankets in dugouts are let down.

Movement ceases, all men standing to "arms," ready to repel attack.

Slow fires are kept up to keep rifles from backing.

AFTER ATTACK

Air tested and mask removed one-half hour after air is found clear.

Dugouts and trenches cleared and ventilated.

Sees that entries are made on cards, casualties separated and sent back.

Report of attack made in writing.

Shell holes covered.

Ordnance cleaned.

149. What is the most essential thing in teaching gas prevention?

Discipline. Training men so that they will adjust respirators when alarm is sounded, and not remove them until given proper authority to do so.

150. What is white star gas?

Combination of 65 per cent chlorine, 35 per cent phosgene.

151. What is the distinguishing color or odor of chlorine? Bromine? Phosgene? Hydrocyanic acid gas?

Chlorine (Cl_2), greenish yellow.

Bromine (Br_2), reddish brown.

Phosgene (COCl_2) smells like bad fish; no color.

Hydrocyanic acid gas (HCN) smells like almonds; no color.

152. Why was it found necessary to instruct all the officers and noncommissioned officers in gas defense?

Gas officer may be killed or transferred, and company would have no one to take his place.

153. How far back has a gas cloud been known to extend, necessitating the wearing of the mask?

Twenty-two miles.

154. How many rattles per mile of front are issued?

Two hundred rattles per mile.

155. How are gas activities carried out against artillery positions?

First, high-explosive shells are fired, which drive men into bombproofs. Then a barrage of gas shells is thrown around battery, making it necessary for gunners to stay in their gas-proof dugouts or else wear their respirators. After several hours of shell it is sometimes followed by a cloud, if wind conditions are favorable.

156. If gas casualties can be largely prevented, why are these activities still resorted to so extensively?

Immense moral effect. Possible that opposing troops are poorly disciplined in gas defense, which means that casualties will surely result. Men can not eat unless taken to the rear and are extremely uncomfortable living in respirators.

157. Why, and for how long a term, is smoking prohibited in the trenches after an attack?

Smoking is not permitted for several hours after an attack because it would irritate the condition of men who might be gassed.

158. Why is it good policy to separate the serious and the slightly gassed?

So that light cases may be attended to first and returned as soon as possible. Also due to the mental effect the suffering of the serious cases would have on the men only slightly gassed.

159. What percentage of all gas cases are returned to the front lines again as effective fighting units, as seem to be shown by statistics?

Practically none, unless slightly gassed.

160. Why and for how long a time are men relieved from duty during an attack?

Men are relieved as soon as possible after a gas attack so that they may clean their equipment in the rear. They are relieved for the regular length of time in force in that sector; usually 24 hours.

161. Describe the gas mask used on horses.

Fits over horse's nose very much like a feed bag. Soaked in chemicals, through which horse breathes and which neutralize gases. No covering for eyes.

162. What is the life of our mask in concentrated gas?

New respirator will last for about 30 to 36 hours.

163. Describe the French "M" type mask, and tell wherein our type is superior.

Layers of heavy gauze, fitting tightly over face, covered with a sort of oilcloth. Has two eyepieces. Gauze is soaked in chemicals, and has unpleasant odor. Breathing, both inhaling and exhaling, is done through fabric of mask, as a result of which the life of chemicals is shortened and respiration becomes extremely difficult, due to dead air space. Our type has no odor, and the intake only goes through chemicals. No dead air space between mask and face. Chemicals last longer due to outlet or gill valve. More comfortable.

164. What particular use has gas hand grenades?

Clearing men out of captured dugouts.

165. Does infantry ever attack during a gas cloud or shell bombardment? If not, why?

No. Life of respirator is conserved by no movement, and movement is difficult with respirator on. England recently sent over a cloud of smoke, and the Germans, thinking it gas, put on respirators, whereupon the English attacked without respirators, with great success.

166. Why is smoke used in connection with gas in clouds? Describe the method.

Can not be distinguished from gas by the eye. Enemy is made to keep respirator on. Smoke is sent over between gas waves, and sometimes mixed with gas.

167. How many masks are carried by each soldier in the field?

Two. One is a reserve mask.

168. What is the most important thing to be remembered at the beginning of a gas attack?

Hold your breath and adjust your respirator.

169. Will our mask protect from gas found in mines, galleries, and in machine-gun emplacements? If not, why?

No. They are carbon monoxide and nitrous fumes, and our respirator is only a filter. Oxygen must be present. In above cases oxygen must be supplied or else life is impossible.

170. Describe the oxygen tank helmet used by the English for miners and sappers and machine gunners, working in inclosed compartments.

Apparatus with two small oxygen tanks strapped on back, and large bag in front containing some caustic soda. Two tubes run up from bag into mouth of wearer. Exhaled air is sent through caustic soda, purified, and rebreathed. Oxygen is fed in from tanks on back as it is needed. No breathing is done through nose, as it is closed by a small clip.

171. What action would you take if your trachea tube were severed during a gas attack?

Hold breath, remove defective respirator, and put on reserve one.

172. What military commands would be utilized to place your men in a two-side square formation?

"Rear rank, right face; column left; march." "Rear rank, halt; left face."

173. What percentage of shells used on the western front are gas shells?
Sixty-five per cent.

174. Why is it necessary to view the mask drill as a military maneuver?
To obtain discipline, which is essential in gas defense.

EDGAR S. LINTHICUM,
Major, M. R. C., Division Gas Officer.

RECENT DATA COLLECTED CONCERNING DEVELOPMENTS IN GAS WARFARE

HEADQUARTERS 79TH DIVISION, N. A.,
GAS DEFENSE SERVICE,
Camp Meade, Md., February 9, 1918.

Recent reports and information from various sources disclose material changes and advance in the use of gas as a weapon in warfare.

It would seem that the Germans on the western front have recently used little gas in cloud attack. The fact that the wind is unfavorable as to direction a large portion of the time may have been conducive to the same, but not wholly so. The prevailing winds during the months of August and September were especially favorable for the enemy. During the month of August, the British forces made an average of 51 attacks per month. These were major cloud offensive operations and entirely separate and distinct for gas-shell usage.

The British are using large quantities of thermite bombs and projector drums filled with oil. These, of course, are incendiary in their effects. The Stokes mortar is being used largely for projecting gas in shells and drums also.

The British are also using a harmless aromatic gas, also smoke candles, and attacking, in infantry rushes, in the midst of the cloud thus created. The Germans are placed under the disadvantage of fighting under the mask. It is predicted that this practice will spread.

During the month of August an average in excess of the latest figures (65 per cent) of gas shells were used by the British. By far the greater portion was used to neutralize enemy batteries. The tendency now is to mix high-explosive shells, which serve to drive the artillerymen into their dugouts. After this result is accomplished, gas shells are mixed in. The gas, being heavier than air, penetrates the stand of the battery, necessitating the wearing of their respirators or retiring to gas-proof shelters. Well-directed gas shells serve to silence artillery positions sooner or later. The wearing of the respirators serves to inhibit free movement, and the guns soon go out of action. On the night of August 21-22, the English fired with gas shells on 19 artillery positions, silencing 18 of them. On the 23d of the same month the Germans opened fire on several English artillery positions with gas shells, drawing a like fire from their opponents. The seeming superiority of the English fire and masks suddenly stopped the German bombardment.

The French are also taking to the use of large-caliber guns in projecting gas shells. Formerly they tended to use mostly the 75-mm. gun, from which a very rapid fire could be obtained.

The Germans have developed several new types of masks. The first one has a facepiece of leather, with the goggles set wide apart, somewhat preventing visual focus and interfering with sight. They are using a new type of antidim lens. It seems to be made of rather a gelatinous substance in disk form, with upturned edges, which tends to absorb moisture, thus preventing "fogging" of eyepieces. They dry out after use. This German mask has no mouthpiece or nose clip, depending entirely upon a close fit against the face. They prohibit wearing spectacles under the mask, claiming that the earpieces prevent the necessary close fit and give rise to "gassings." They recommend that the spectacles be fastened on with tape. The other mask that they have developed is really not a mask at all. It is a small canister, containing chemicals, to which they have recently added ground pumice stone, to which is fitted a metal mouth tube resembling largely our own rubber mouthpiece. Attached by a string is a nose clip. There is no facepiece or goggles; it being the intention to supply men with this apparatus whose free movement would be inhibited by goggles. It is carried in a specially constructed pocket of the coat. This is carried in addition to the regular issue mask.

The French have also developed a new box respirator especially to be used by the artillery. It is a wide departure from any yet in common use. The canister is attached on the wearer's back with tube leading over left shoulder to facepiece. It has no mouthpiece or nose clip. The connecting tube bifurcates, entering just below each eyepiece. This, it is hoped, will prevent "fogging." It is cumbersome and apparently heavy. The gill valve sticks straight up from the point at which the air tube enters the facepiece.

In the operations on the Austro-Italian front, the enemy has used gas in liberal quantities, in both cloud and shell. In fact, the Italian retreat was due to the use of poisonous gases.

The Germans are using high-explosive shell into which is incorporated a bottle (glass) containing a powder, which upon bursting disseminates this chemical, causing sneezing and coughing. The shell is a combination high explosive and chemical, or gas shell.

The Italians have improved their mask somewhat, it would seem. This mask resembles very closely the French "M" type.

The Russian respirator differs entirely from any other type. It has a rubber facepiece which fits tightly over the whole head, covering also the ears. To the front of this facepiece is attached the canister directly, resembling, in a way, the German mask. The canister is larger than our own and has an inlet and outlet valve in the bottom of can. These valve openings are about $1\frac{1}{4}$ inches in diameter, and have two tubes protruding from the lowest part of can, which when not in use are covered with rubber caps. The mask is said to be very uncomfortable.

The Germans, during the month of September, attempted to use gas in cloud against a sector of the French front. The French sent over a raiding party which was so fortunate as to entirely frustrate the attempt, destroying the cylinders.

The Germans are also using a new Flammenwerfer apparatus consisting of a nitrogen tank placed within a tank containing oil, the apparatus being carried on the back of the operator. This duty is so hazardous and so little sought that it is said the Germans are placing men on this duty as a punishment.

The Germans are also using a new deodorizing cartridge to clear out dugouts quickly. They are fired from a flare pistol. They contain dimethyl aniline. They also use this pistol for firing a cartridge into a dugout to test out the fit of masks. Here they use a bulb containing a lacrymator. This method of clearing dugouts is not satisfactory. It, in itself, creates an irritating gas. The Germans claim this gas to be nonpoisonous though.

In September the British carried out 51 major gas operations. The Germans also have a form of projector now. The reports from captured documents tend to show that the Germans are getting the worse of gas. They state that as many casualties are caused by gas as by artillery. Their losses seem to have been particularly heavy from this weapon during the summer months. They state that you may expect 15 per cent of the total number of troops engaged to be gassed more or less severely. Their losses are probably due, it would seem, to the large influx of fresh troops and the character of their masks at this time. There seems to be a shortage of rubber from which to manufacture efficient protectors. They say that not more than 3 per cent of your moderate and severe cases return to the fighting troops. The 14th Bavarian Regiment lost 204 men killed and 554 casualties during August, it is reported. Some companies' losses ran all the way to 80 per cent. In one hospital, out of 2,000 cases, 986 were the result of gas. Prisoners report much malingering among the enemy troops.

In October the standing orders within the theater of operations was changed, in so far as wearing the masks was concerned. The new positions areas follows: Alert, from the front line to 2 miles to the rear; ready (carry), from 2 miles to the 5-mile limit; precautionary, from 5 to 12 miles. This position consists in having the mask off the person but in the near vicinity, so that a speedy adjustment is made.

During this month (October) the British liberated 260 tons of gas in 40 clouds attacks. Incendiary bombs were also used successfully.

The British are still using the P H helmet outside of the first 5 miles. The British do not enter time on the record card for drill any more, except in the following way: They record one hour's time per week for mask drill, figuring on two hours of drill, but one hour of actual wear.

In July the Germans are reported to have pulled off more cloud attacks than for months; the reason being, apparently, that the wind was most favorable from their viewpoint. During the Italian drive they also used it in considerable quantities, as previously stated.

The English are issuing 200 rattlers to the mile of front. The fact that the noise created by these instruments so closely resembled machine-gun fire had for a time placed them in disrepute, save for artillery. The above would seem to indicate that they are coming into vogue again.

The British permit the chinstrap to be used under point of chin now. Heretofore, this was only permitted among the bombers. They also advise adjusting the respirator when gas shells are detected, and when this operation is completed to shout "Gas shells."

The British advocate knocking the helmet or hat off with the left hand prior to adjusting the mask. The French, on the other hand, advocate that the hat be held between the knees or, if armed with a rifle, that this weapon be held thus, placing the hat or helmet thereon on the muzzle. Hats or helmets when thrown off in the trenches or on the ground are frequently rendered unserviceable on account of the mud, etc. We will teach in this division the French method, and all classes and individuals will conform to this order. The drill must be made uniform and executed as a military maneuver, at strict attention.

EDGAR S. LINTHICUM,
Major, M. R. C., Division Gas Officer.

A SUGGESTED ORGANIZATION OF THE GAS SERVICE OF THE AMERICAN ARMY

[Prepared for the chief of staff, American Expeditionary Forces, * by James Robb Church, major, M. C.]

1. Pursuant to verbal orders, I submit the following scheme for the general organization of a gas service for our Army.

2. Of necessity, the report does not deal with final details under many of the subheads. It is not believed that this would be practical, and the appointment of suitable heads of subordinate sections should carry with it the responsibility of the organization, both as to personnel and material, for the competent execution of the duties falling to that section.

3. In outlining this organization, both French and British methods have been taken into consideration and, where deemed applicable, adopted for our own use.

4. It seems to me of first importance to realize that with us the service will be under different conditions from either French or British. The former are operating mainly on their own territory, and the British separated by only a short distance from their central seat of government. For either of them, therefore, the correlation of the field force and that of the interior is a relatively simple matter. In our own case the service will lie on both sides of the Atlantic, and it seems important to determine where the active, dominant authority should lie.

5. Inasmuch as all orders or plans emanating from the United States must be based on reports from this side, it is believed that final decision and authority should lie in France; that is, with the commander of the American Expeditionary Forces. The section of the service operating in the United States should not only cooperate with the section here, but go further and subordinate its views to actual experience gained at the front.

6. I doubt if even now the majority of people understand the importance of chemical warfare by poisonous gases and allied special methods of destruction in modern warfare, or the infinity of detail which is requisite to use them in offense or to protect against attacks with them. It is certain that these methods must be counted as established weapons in modern warfare and a knowledge of them acquired not only for the present conflict but for wars which may yet come. Without this precise knowledge and intelligent preparation, no modern army is an effective offensive force nor can it withstand attack by these methods.

7. We have now the advantage of two years' experience of our Allies, and if we profit by this our casualties from this source should be limited and our offensive strength equal to theirs plus what we can add by our own ingenuity.

8. Due to the highly technical character of this form of warfare, a special organization is as essential, perhaps more so, as that required for the existing special services—the Ordnance, Artillery, Signal Corps, or Medical Corps. It is a service apart from others and yet drawing into its completed unity elements from many of the others; so the French have built it up and so the British.

While the service must be made up of personnel drawn from the different arms and corps of the service, it is not believed that the best results will eventuate from assigning definitely this special work in whole or part to any particular arm or corps.

It is logical that this work should be directed by a head drawn from the arm or corps most interested, but this arm or corps should not be directly charged with the carrying out of it nor assume the responsibility. The general responsibility should focus in the director of gas service.

9. The diagram appended shows the general outline of the service as proposed and the relation as to orders and reports.

It is not practicable or necessary to indicate the more subordinate personnel; this is a matter to be decided by the section heads, subject to the approval of the director of gas service.

The following discusses, in more detail, the elements shown in the scheme:

* Appendix No. 5, History of Chemical Warfare Service, American Expeditionary Forces, Vol. I, 87. Copy on file, Historical Division, Army War College.

10. The service shall consist of a director of gas service at the head of an operative and advisory personnel as hereinafter described.

(a) For the offensive use of modern chemical methods of warfare, there shall be a number of specially trained companies under the command of the director of gas service, and known as the "gas brigade" and officered in the usual manner.

(b) For advisory purposes there shall be a chain of officers of the gas service, under the command of the director of gas service, attached to the staff at each headquarters from that of the commander in chief down to divisional headquarters. By this means an efficient and uniform policy with regard to gas questions can be maintained throughout the entire expeditionary force, and therefore no fresh instructions are required by units when they are transferred from one formation to another. Below the divisional unit there shall be specially designated officers and noncommissioned officers of the regular formations, whose additional duty will be to assist the commanding officer of that unit in carrying out gas defensive measures.

11. While the final responsibility of all acts rests with the commanding officer of each formation, yet it shall be incumbent on him to request and consider the advice of his accredited gas officer; that advice should only be disregarded with due consideration, and the grounds for this disregard immediately reported to the commanding officer of the next higher formation.

12. The commanding officer of a unit to which a gas officer is assigned shall report any inefficiency of the gas officer to the superior officer of the gas service and to his own superior officer, who will take appropriate steps to bring the same to the attention of the director of gas service.

13. All gas officers shall be furnished with and wear an appropriate brassard designated by the director of gas service.

14. *Duties of the director of gas service.*—(a) There shall be a director of gas service (D. G. S.), with the rank of a general officer.

(b) The director of gas service shall be in command of all officers and other ranks assigned to the gas service, whether for offensive, protective, or investigation purposes.

(c) The director of gas service shall sit on the general staff of the commander in chief of the expeditionary force and there give advice on all questions connected with chemical warfare, both offensive and defensive.

(d) The director of gas service shall request the assignment of such officers and enlisted men as he needs for the administration of his department. He shall have authority to decide the fitness of any officer for the duties to be performed in his organizations. Promotions or changes within his department shall be made on his recommendation.

(e) After the adoption of any general plan or policy in regard to chemical warfare by the commander in chief and general staff in consultation with the director of gas service, the latter shall be responsible for the carrying out of such plans and policies by the means of the gas service organization.

(f) The director of gas service, with the advice and consent of the commander in chief and general staff, shall transmit to the home director of gas service (H. D. G. S.) the final decision on all questions concerning chemical warfare, both offensive and defensive. The closest harmony and cooperation between the director of gas service and the home director of gas service should exist, but if differences of opinion arise the final decision must perforce be in the hands of the commander in chief of the expeditionary force through the director of gas service.

(g) Such investigation of problems as the director of gas service desires carried out at home shall be promptly done by and through the home director of gas service.

(h) All supplies requested by the director of gas service shall be furnished as soon as possible by the home director of gas service.

(i) All suggestions of whatever nature received by the director of gas service from the home director of gas service shall receive his immediate attention and, if concurred in, be adopted.

15. *Duties of the deputy director of gas service (D. D. G. S.).*—(a) There shall be a deputy director of gas service with the rank of a field officer.

(b) The deputy director of gas service will be second in command to the director of gas service in the gas service and shall aid and assist the director of gas service in carrying out his duties.

(c) In the absence of the director of gas service, the deputy director of gas service will perform all the duties assigned to the director of gas service.

(d) The deputy director of gas service shall sit on the general staff but, when his superior officer is present, will have no decisive voice, although his opinion should be requested and freely given.

16. *Duties of the assistant director of gas service (A. D. G. S. (D)) defensive.*—(a) There shall be an assistant director of gas service for the defensive and protective side of chemical warfare, of the rank of a field officer.

(b) The assistant director of gas service (defensive) will rank next to the deputy director of gas service in the gas service. In the prolonged absence of the deputy director of gas service, or the prolonged adoption of the duties of the director of gas service by the deputy director of gas service, the assistant director of gas service (defensive) will fulfill the duties of the deputy director of gas service.

(c) The assistant director of gas service (defensive) will sit on the general staff in case of prolonged absence of the director of gas service or deputy director of gas service on the invitation of the commander in chief.

(d) The assistant director of gas service (defensive) shall be stationed at the headquarters of the gas service and assist the director of gas service in formulating all defensive measures and policies and shall be in direct charge of the work of the chemical advisers situated at the headquarters of the various formations of the expeditionary forces. He shall supervise the training in gas defensive and see that the orders of the director of gas service given therefor are uniformly carried out in all formations of the expeditionary forces.

(e) The assistant director of gas service (defensive) will establish and have direct charge of a base school for the teaching of officers and noncommissioned officers who will be assigned to the gas service, as well as such other officers as it may from time to time appear advisable to instruct. For this purpose he shall be provided with appropriate personnel and equipment.

17. *Duties of chemical adviser of the army (C. A. of A.).*—(a) There shall be a chemical adviser of the army (C. A. of A.), attached to each army headquarters, with the rank of major. He must be a man technically conversant with chemistry.

(b) The chemical adviser of the army shall sit on the army staff and give advice on all questions connected with chemical warfare.

(c) As an officer of the gas service he shall be departmentally under the assistant director of gas service (defensive) at general headquarters and will deal with all technical matters with the chemical advisers of the corps and division as the ranking officer of the gas service within the army.

(d) Under the general staff at army headquarters the duties of the chemical adviser of the army shall be:

(aa) To exercise general supervision over the training in antigas measures of all troops included in the strength of the army or serving in the army area.

(bb) To advise the staff on all questions connected with defensive measures against gas and on all technical matters concerned with the characteristics of the materials used in chemical warfare.

(cc) To advise on technical points connected with the offensive use of gas and smoke, except in regard to operations conducted by the special brigade. He may suggest the practicability of using the special brigade, but the commanding officer of the special brigade attached to the army should give his own advice on this subject; there should be the closest cooperation between the chemical adviser of the army and the commanding officer of the special brigade in those matters where their respective functions approach each other; neither, however, has authority over the other.

(dd) Close cooperation should exist between the chemical adviser of the army and the commanding officer of the artillery, and the chemical adviser of the army should be consulted as to the best chemical means of attaining an object; i. e., the gas to be used, the number of shells to be required, and the effects of terrain and weather. Therefore he should be invited to be present at the time of preparation of programs for the artillery whenever the use of gas shell is to be considered.

(ee) To advise and cooperate with the supply officer of the gas service in the reserve stock issue and distribution of all gas appliances needed by the army; to draw such supplies as he shall need to meet the requirements adopted by the gas service, requests for additional supplies to be forwarded through the proper channels to the director of gas service.

(ff) To collect and transmit to the laboratory, for examination, all kinds of enemy chemical appliances and projectiles. To insure that this latter duty is properly and efficiently executed, he shall have authority to inspect all captured appliances, etc., at dumps and elsewhere, and to forward what is, in his opinion, worthy of examination.

(gg) To investigate and report both to his staff and to the director of gas service (through the assistant director of gas service (defensive)), on all cloud gas and important gas shell attacks by the enemy.

(hh) To cooperate with the intelligence department in collecting from prisoners and other sources information relating to enemy gas warfare and to the effects of our own gas attacks.

18. Should an antigas training school be required in the army organization, it shall be the duty of the chemical adviser of the army to direct the school, for which purpose the necessary personnel and equipment shall be furnished him.

19. *Duties of chemical adviser of the corps (C. A. of C.).*—(a) There shall be a chemical adviser of the corps (C. A. of C.) attached to each corps headquarters, with the rank of captain.

(b) The chemical adviser of the corps shall sit on the corps staff and give advice on all questions pertaining to chemical warfare.

(c) As an officer of the gas service, he will be departmentally under the chemical adviser of the army, and finally the director of gas service at headquarters. He shall deal with all technical matters with the chemical advisers of the divisions as the ranking officer of the gas service within the corps.

(d) The further duties of the chemical adviser of the corps shall be analogous to those described in sections (aa) to (hh), paragraph No. 17, of this document, applicable to the chemical adviser of the army.

20. *Duties of the chemical adviser of the division (C. A. of D.).*—(a) There shall be a chemical adviser of the division (C. A. of D.) attached to each divisional headquarters, with the rank of captain. He shall be a man technically conversant with chemistry.

(b) The chemical adviser of the division shall sit on the divisional staff and give advice on questions pertaining to chemical warfare.

(c) As an officer of the gas service he shall be departmentally under the chemical adviser of corps and, finally, the director of gas service at headquarters.

(d) Under the staff at divisional headquarters he shall—

(aa) Exercise general supervision over the training in antigas measures of all troops included in the strength of the division.

(bb) Be in executive command of the divisional antigas school and personnel attached to the school for duty and be responsible for the special antigas training carried out there, for which purpose he shall be furnished adequate personnel and equipment.

(cc) Advise the divisional staff on all questions affecting the protection of the troops against hostile chemical warfare, the location of alarm devices, and the ordering and counter-ordering of gas alert, etc.

(dd) Advise and cooperate with all commanders of units within the division on all protective measures against hostile chemical warfare and in their utilization of battalion gas officers and company gas noncommissioned officers, according to the manner adopted by the gas service.

(ee) Direct and assist the battalion gas officers and the company gas noncommissioned officers in the establishment and execution of the gas training and gas protective measures adopted by the gas service.

(ff) Cooperate with and advise the appropriate supply officer of the gas service of the probable needs of the division as to reserve and distribution of gas appliances. On his order such stores shall be issued by the supply officer as will meet the requirements adopted by the gas service. Requests for additional material shall be forwarded by the chemical adviser of the division, through the proper channels, to the director of gas service.

(gg) The chemical adviser of the division shall be advised daily by the Medical Corps of the number and location of all gassed cases. This information shall be reported through the intermediate channels of the gas service to the director of gas service.

(hh) The chemical adviser of the division shall be immediately notified of any gas attack so that he may arrive on the spot as soon as possible for the purpose of investigation and to give advice. This information shall be reported through the intermediate channels of the gas service to the director of gas service.

(ii) He shall investigate and report to the divisional staff and to the chemical adviser of corps all enemy attacks made with the aid of chemical methods.

(e) The position of the chemical adviser of the division is one of great importance, as he forms the direct line between the gas service and the units, and the gas defense of the division depends greatly on the energy and ability of its chemical adviser.

(f) It is imperative that the chemical adviser of the division shall inspect units both in and out of line as soon after an attack as possible. On these inspections he should be accompanied whenever possible by the battalion gas officer and gas noncommissioned officer of the unit visited. He should investigate the state of gas training and inspect antigas appliances.

(g) He shall be assisted in his duties by the necessary personnel and equipment. This would probably consist of a lieutenant and three noncommissioned officers, aside from the personnel necessary to conduct the divisional school, which would require a lieutenant in charge and six noncommissioned officers and four fatigue men; the equipment would consist of an office and office appliances, a lecture tent, a store tent, and a system of training trenches.

21. *Battalion gas officer (B. G. O.).*—(a) An officer in each battalion, or corresponding unit of the special service, shall be designated as the battalion gas officer (B. G. O.) by the commanding officer of the regiment, on recommendation of the battalion commander.

(b) The battalion gas officer should, if possible, be a senior lieutenant; he must have taken a course of instruction at an antigas training school.

(c) The battalion commanding officer shall be responsible for the proper fulfillment of the duties of the battalion gas officer and, therefore, for the protection of his men; the commanding officer will see that the necessary orders are issued so that the requirements of the gas service can be efficiently met by the battalion gas officer. The fact that there is a specially designated battalion gas officer does not absolve the commanding officer of the battalion for failure or neglect in the carrying out of the required antigas measures.

(d) The battalion gas officer will receive directions as to the proper methods of training the troops and the use of protection and of antigas appliances from the chemical adviser of the division. He will, whenever practicable, accompany the chemical adviser of the division on rounds of inspection.

(e) The battalion gas officer will advise with the battalion commanding officer and the chemical adviser of the division as to the required amount of time to be devoted to antigas drill and see that the company noncommissioned officers efficiently discharge their duties.

(f) The battalion gas officer will, in conjunction with the company noncommissioned officers, inspect the training and drill of the men and the antigas appliances issued, and report any faults or deficiencies to both the battalion commanding officer and to the chemical adviser of the division.

(g) The battalion gas officer shall requisition of the chemical adviser of the division any antigas stores required; immediately on the approval of the chemical adviser of the division, the supplies so requisitioned shall be issued by the supply officer of the gas service.

(h) The battalion gas officer shall collect as much information as possible during and immediately after an attack by the enemy, in which chemical methods of warfare were used against his unit. He should make and send a report of such information, as soon as possible, to the chemical adviser of the division, together with the written notes of the company noncommissioned officers, as well as to the battalion commander.

22. *Company gas noncommissioned officers.*—(a) In each company there should be several noncommissioned officers who have attended a course in the antigas training school. The best fitted of these men shall be designated as company gas noncommissioned officers by the battalion commanding officer on the advice of the battalion gas officer. They shall perform special duties in regard to training the men in the use of their protective and other antigas appliances and in the store and care of the same, as may be delegated to them by the battalion gas officer.

23. *Chemical adviser, lines of communication. (C. A. of L. C.).*—(a) There shall be a chemical adviser of the lines of communication of the rank of major, attached to headquarters, lines of communication; in the gas service he shall rank equal to the chemical adviser of the Army. He shall sit on the staff of the lines of communication.

(b) The chemical adviser, lines of communication, shall:

(aa) Supervise any antigas school established at base depot or in the lines of communication area at which all drafts and reinforcements are issued and equipped with respirators and given a short course of instruction in their use before proceeding to army areas.

(bb) Supervise and control the work carried out in connection with the repair of antigas appliances at the bases.

(cc) Advise the director of ordnance service and the supply officer of the gas service and the base along the lines of communication in all technical matters concerned with the storage and turnover of gas-service supplies.

(dd) Direct the protection of the personnel handling lethal and lacrymatory shell, gas cylinders, etc., on lines of communication.

(ee) Satisfy himself with the efficiency of the antigas equipment of units arriving in France.

24. The director of gas service may establish a chain of chemical advisers in the lines of communication corresponding to the chain proceeding down through the armies to the divisions, provided, in his opinion, the need for the same should arise.

25. *Assistant director of gas service (offensive) (A. D. G. S.).*—(a) There shall be an assistant director of gas service (offensive) for the offensive side of chemical warfare of the rank of field officer.

(b) The assistant director of gas service (offensive) will be stationed at the headquarters of the gas service and assist the director of gas service in formulating all offensive measures and policies and will be in administrative charge of the special gas brigade.

(c) He will make himself thoroughly conversant with all the special offensive methods of the Allies and the enemy and shall be in constant consultation with the research department in an attempt to improve the effectiveness and scope of the chemical methods of warfare.

(d) The assistant director of gas service (offensive) will detail companies of the special gas brigade, under the command of a major, to the various armies, there to give advice on and to specially carry out such offensive measures as the army staff desire. The major in charge of special companies shall work in close cooperation with the chemical adviser of the army, but neither shall be subordinate to the other. It is advisable, whenever practicable, that their respective departments be in close proximity. Furthermore, there must always be the closest cooperation between the commanding officer of the special companies and the artillery commander and frequent consultation one with the other should occur. When infantry operations are to form a part of the program, consultation with the infantry commander should always take place. Only by such consultation will it be possible to make the fullest use of these new methods of warfare.

26. *Director of the laboratory (D. L.).*—(a) There shall be a director of the laboratory, with the rank of field officer.

(b) The director of the laboratory shall be in complete charge of all laboratories established in France under the control of the director of gas service.

(c) He shall be given complete authority and means, both personnel and material, to establish and maintain research laboratories of the highest efficiency for studying all appliances used in chemical warfare and attempt to increase their scope and efficiency. He will also test the protective apparatus and pass on its good and satisfactory character and condition.

(d) There shall be a physiologist conversant with the theories and mechanics of respiration attached to the laboratory.

(e) There shall at all times be the closest cooperation between the director of the laboratory and other members of the staff of the gas service. The laboratories shall be available for the immediate investigation of any new problems that may develop.

27. *Intelligence officer.*—(a) There shall be attached to the staff of the director of gas service an intelligence officer, whose duties shall be to collect from the general intelligence service the information specially pertinent to chemical warfare. He shall correlate all such information and from time to time make reports to the director of gas service. He shall, when occasion arises, aid in special investigation of prisoners. He must be thoroughly conversant with the German language.

28. *Liaison officer.*—There shall be attached to the staff of the director of gas service one or more liaison officers in order that full information concerning the methods of our Allies in chemical warfare can be obtained. The director of gas service shall be free to appoint liaison officers to be permanently assigned to various gas departments of our Allies; in return he shall welcome the assignment of such officers to our department.

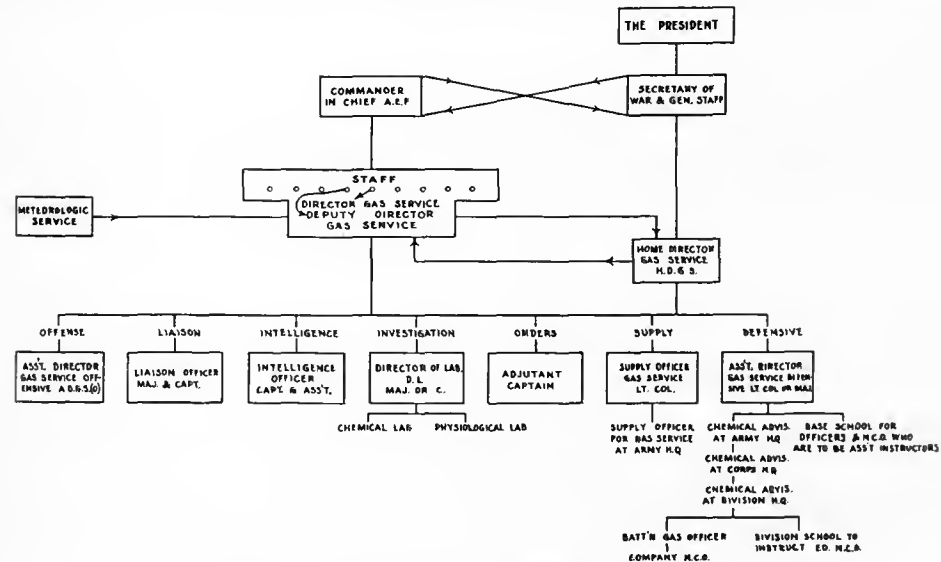
29. *Supply officer.*—(a) There shall be a supply officer, with such personnel as may be deemed necessary.

(b) The supply officer shall have station at the base, or one of the bases, and shall draw, as far as possible, all supplies needed for the gas service of the expeditionary force from a similar officer with the home gas service or from an appropriate officer with the American Expeditionary Forces.

(c) There shall be a gas supply officer with each army and with each division of an army, and supplies shall be drawn by each unit from the one above it, thus providing a supply by "echelon." This to be effective provided it does not conflict with existing methods of supply.

30. *Adjutant, duties of.*—(a) The duties of the adjutant shall be the general supervision of records and such other duties as may be assigned to him by the director of gas service.

31. *Meteorological service.*—(a) The meteorological service should not be a part of the gas service, but it should work in the closest harmony and cooperation with it. The closest affiliation should exist with the meteorological services of the English and French.



Organization of Gas Service prepared by Maj. J. R. Church, M. C.

(b) The use of gas is absolutely dependent on the direction and strength of the wind and on its probable duration. Expert advice on meteorological conditions should be immediately available to all officers of the gas service. Therefore, this service should have its headquarters at the general headquarters, and forecasts should be issued three times a day to the gas headquarters, to armies, to corps, and to divisions.

(c) A meteorological officer should be established at each army headquarters, and a series of meteorological stations at situated points along the line.

(d) Warning should be sent to each formation when the wind enters a dangerous quarter as regards gas attacks by the enemy. The forecasts should contain special reference to surface winds.

JAMES ROBB CHURCH, *Major, M. C.*

HEADQUARTERS AMERICAN EXPEDITIONARY FORCES,

July 26, 1917.

GAS DEFENSIVE ORGANIZATION OF THE BRITISH ARMIES IN FRANCE*

The general organization of the gas services as a directorate under general staff is shown in the attached diagram (A) [lacking].

Both the offensive and defensive services are under the director of gas services and occupy the same headquarters at G. H. Q.

General organization of defensive service.—The principle of the organization is to have one or more officers of the gas services attached to the general staff at each headquarters in the chain of command down to divisions, who are responsible for advising the various branches of the staff on all questions connected with gas defense, and also for the necessary departmental administration.

By this means a uniform policy with regard to gas defense is maintained throughout the armies and no fresh instructions are required by units when they are transferred from one formation to another.

The full establishment at each headquarters is given in Appendix I, and it is summarized in the following diagram (B) [lacking].

Under the new establishment all officers are transferred to the Royal Engineers in order to unify the service and to facilitate transfers to and from special brigade, R. E., so that all officers on the defensive side may have a thorough acquaintance with offensive methods.

In choosing officers for the service the three main qualifications sought for are:

- (1) Experience in the line.
- (2) Special knowledge of chemistry.
- (3) Teaching experience.

Of these, (2) is not essential for a divisional gas officer, but it is a great advantage, and without it he can not be promoted to be a corps or army chemical adviser, for whom a university training in chemistry is essential. Officers selected are transferred to the special brigade, R. E., and after three months' work in the line with a special company engaged in gas offensive operations are considered as vacancies on the defensive side as they occur.

The general scope of the work of chemical advisers and gas officers is:

- (1) Advisory.
- (2) Administrative.
- (3) Instructional.
- (4) Inspectional.

Their duties will be considered in detail at each headquarters.

At General Headquarters.—The director of gas services acts as adviser to the general staff and to other branches of the staff on all questions connected with gas defense. In addition he is responsible for the administration of the gas services, appointments being made on his recommendation.

He is assisted by the A. D. G. S. (B) and the D. A. D. G. S. The A. G. D. S. (B) is responsible for correspondence with the various branches of the staff, and with the chairman of the antigas committee and chemical adviser, G. H. A., home forces. The D. A. D. G. S. is responsible for personnel and for keeping records of:

- (1) Information about chemical substances in gas warfare.
- (2) Information about antigas appliances.
- (3) Hostile gas and gas shell attacks.

Relations with war office with regard to antigas appliances.—At the war office the D. G. A. M. S. is responsible for the protection of the troops against gas. The antigas committee, consisting of chemists, physiologists, and members of the A. M. S., advises him on technical points connected with antigas appliances. The chairman of the antigas committee controls the factories engaged in making antigas appliances, also the antigas laboratory at Millbank, where the necessary experimental work is carried out. Questions relating to the protection

* Appendix No. 6, History of Chemical Warfare Service, American Expeditionary Forces, Vol. 1, 100, Copy on file, Historical Division, Army War College.

of the troops in France are referred by the D. G. S. to the D. G. A. M. S., or his deputy, the chairman of the antigas committee. Questions of policy are settled by agreement between the D. G. A. M. S. and D. G. S.

Relations with war office with regard to training of drafts and reinforcements.—From time to time recommendations are made by the commander in chief to the war office as to the home training necessary for drafts and reinforcements.

The chemical adviser, G. H. Q., home forces, advises the general staff on questions of gas defense. He is in constant touch with the D. G. S. in order to make the home training coincide as closely as possible with the training in France.

Physiological adviser.—A physiologist with military experience is attached to the H. Q. of the gas directorate to act as liaison officer between the D. G. M. S. and the D. G. S. and the physiologists working in England.

This officer will:

- (a) Advise the D. G. S. on physiological points.
- (b) Collect all medical reports and observations both from workers in the B. E. F., at home, and in allied countries, bearing on the physiology and pathology of gas cases for the D. G. M. S.
- (c) Report to D. G. M. S. all developments of gas warfare as they bear on medical work and report to D. G. S. all development of medical work on gas cases that have a bearing on gas warfare.
- (d) As far as possible, cooperate with consultants and be available at the request of the D. G. M. S. for any special research or investigation in treatment, or as an adviser if required.

Meetings of chemical advisers at G. H. Q.—Meetings of chemical advisers of armies, L. of C., cavalry corps, and the director and assistant director of the central laboratory are held fortnightly at G. H. Q. to discuss questions that arise with regard to the organization of gas defense and the protective appliances. A copy of the minutes of one of these meetings is given in Appendix I [not attached].

[Submitted by Maj. Charles Flandin, of the French gas services]

It would be wrong, however, to pick out special points and simply combine them. Knowing what others have done, we have to ascertain along what lines our plans should be directed. Following are the points which should be examined before issuing definite proposals:

The two principal features of the gas organization in the German Army are the following:

(b) **Specialization.**

WAR OFFICE IN BERLIN, GENERAL STATION FOR CHEMICAL QUESTIONS

RESEARCH	WORKS	OFFENSIVE CORPS	ADVISERS
Laboratories.....	Factories control	Special pioneers for gas clouds	3 groups of Artillery
	Filling stations		Gas schools
	Gas masks		Gasschutz
Experimental grounds	Oxygen sets, etc.		Offiziere
			Army (staff officer)
			Army corps (staff officer)
			Troop officers, divisional
			regimental
			battalion

For using gas in warfare, officers have been selected among the chemists and meteorologists. Most of the men in special companies were employed in chemical plants during peace times.

* Appendix No. 7, History of Chemical Warfare Service, American Expeditionary Forces, Vol. I, 103. Copy on file, Historical Division, Army War College.

So we do not find in the German Army the same sharp distinction between war office and G. H. Q. as in the other armies, at least in regard to the gas service.

2. *Gas organization in the French Army.*—When the first gas cloud was sent over by the Germans on April 22, 1915, neither the French nor the British had warning, and gas organization had to be arranged at once.

The most urgent question was that of protection against gas; afterwards there arose the question of developing the offensive. The present scheme of organization is as follows:

"La direction des services chimiques" is part of the "Ministère de l'Armement." Two departments of the "direction des services chimiques" deal, respectively, with research and manufacturing. These are "inspection des études et expériences chimiques," and "direction du matériel chimique." The latter takes up all administrative questions; i. e., expenses for the former. "L'inspection des études et expériences chimiques" has two branches, two committees, called "Section d'Aggression" and "Section de Protection."

Besides research work carried on at laboratories and experimental fields, the "inspection des études et expériences chimiques" has the responsibility for the gas schools attached to all "dépôts de troupes" behind the lines, as well as the "centre d'instruction" and military schools for officers and noncommissioned officers. The "inspection" has to collect information on the effects of gas in warfare and to control the means of protection against gas. Therefore, it is in constant liaison with the armies, sending out to the front a special officer (Major Flandin) each time an important gas attack occurs. The "inspection" has also to control the manufacture of gas, gas and flame weapons, the filling of gas shell and bombs, the manufacturing of gas masks, oxygen apparatus, and other means of protection. Therefore, it is in constant touch with "la direction du matériel chimique," which is in charge of everything concerning manufacture and works. The latter is at the same time under control of "la direction des services chimiques" and part of "le sous-secrétariat des fabrications au Ministère de l'Armement," which controls all kinds of works, workers, raw materials, etc.

From the above-mentioned particulars it may be inferred that "la direction des services chimiques" assumes all scientific and technical works, issues weapons, distributes directions as to using them properly, and looks after the training of the men in protection against gas.

The actual use of gas in warfare is under the sole control of G. H. Q. Cylinder gas is delivered by special companies—two groups of two battalions (each group being attached to a "groupe d'armée") are actually under command of a colonel attached to G. H. Q.

Each battalion has two companies and a park. There are companies for repair, and so forth. Each company has everything at hand to install cylinders in the trenches and send out gas clouds, even being provided with a meteorological station for wind observation. One officer in each high staff is in charge of gas operations, in addition to his other duties. Gas shell are entirely in the hands of the artillery. Special directions for the use of gas shell have been given to gunners by pamphlets issued by "l'inspection des études et expériences chimiques" (Capitaine Nebout), at the request of G. H. Q., and special lectures are delivered to gunners in Paris and in the armies on the use of gas shell.

Protection against gas, especially by means of gas masks, was for a long time under the sole responsibility of troop officers and medical officers. Lately it was decided that in each regiment an "officier de protection contre le gaz," commonly called "officier gazier," would be in charge of everything concerning protection against gas; e. g., distribution of gas masks, training, inspection, gas chambers, sprayers, protected dugouts, etc.

In each "groupe d'Armée" the "centre médico-légal," including several officers, is in charge of diffusing instruction and information, collecting information, making post-mortem examinations, etc. These officers are in touch with G. H. Q. and with "l'inspection des études et expériences chimiques." Also in each "groupe d'Armée" an "officier chimiste" attached to the "inspection de l'Artillerie" has to collect blind German gas shell and collect all information concerning the gas used by the enemy.

From the whole organization one may infer that many people have to deal with gas, but that nearly no one has to deal only with gas. However, results have not been bad. Gas is being used more and more every day and is killing more and more Germans. Losses from German gas are becoming lower, although gas attacks are gaining in intensity. (The table of French organization is presented on following page.)

MINISTÈRE DE L'ARMEMENT.
DIRECTION DES SERVICES CHIMIQUES.

SOUS SECRÉTARIAT DES
FABRICATIONS

INSPECTION DES ÉTUDES ET
EXPÉRIENCES CHIMIQUES

DIRECTION DE MATÉRIEL CHIMIQUE

Fabrications
Administration

Section d'Aggression

M. Moureu (laboratoire)
M. Delépine (laboratoire)
M. Lebeau (laboratoire)
M. Simon (laboratoire)
M. Job (laboratoire)
M. Urbain (laboratoire)
M. Kling (laboratoire)
M. Bertrand (laboratoire)
M. Grignard (laboratoire)

Section de Protection

M. Vincent
M. Achard (laboratoire)
M. Desgrez (laboratoire)
M. Lebeau (laboratoire)
M. Bertrand (laboratoire)
M. Pellerin (laboratoire)
M. Bouzet (laboratoire)
M. Flandin (laboratoire)
M. Doppler (laboratoire)

Cours de gaz

Contrôle des
fabriques

Instruction et
contrôle de
l'instruction
à l'arrière

Liaison
avec les Armées
Françaises et
alliées

Major Flandin
Captain Nebout

M. Mayer, laboratoire de physiologie

G. H. Q.

1^{er} Bureau,
Administration

3^e Bureau,
Opérations

GROUPE D'ARMÉE

Officier de gaz Centre médico-légal Officier chimiste

ARMÉE

CORPS D'ARMÉE

Officier de gaz,
3^e Bureau

Officier de protection de gaz,
4^e Bureau

Division de régiment

Officier de protection de gaz

3. *Gas organization in the British Army.*—This is plainly described in Lieutenant Colonel Hartley's report handed to Captain Boothby.

The main characteristics of the British organization are the full independence between the service in France and the service in England. Also in England there is absolutely no touch between offensive and defensive, and thus the same work has sometimes to be done twice or more, and therefore there is a waste of time, waste of materials, and waste of men. However, I can not say enough in praise of the organization of the gas service in the army fighting in France, as I know personally of the excellent results both on the offensive and defensive side in the last months.

4. *Requirements of gas services in a modern army.*—Present warfare is so different from former fighting that the directive principles of organization have also to be absolutely different. As regards gas, it seems to me that the organization ought to be less military than industrial. The results will be in direct proportion to the amount of gas properly sent out against the enemy. Therefore, the control of gas warfare has to be in the hands of those who know everything about it and can establish the best way to use it properly. Of course, these peoples have to know enough of the battle field to be able to give directions that may be actually followed in the field. Therefore, we are coming to the realization that the director of gas service has to be at the same time a chemist, a physiologist, a trader, a soldier, and, as soldier, to know infantry as well as artillery and tunneling work. As it is perhaps impossible to find such a broadly trained being, it means that the direction of gas service has to include chemists, physiologists, gunners, pioneers, and manufacturers. The second important point is that gas weapons have to be followed from the laboratory where they are invented to the factory where they will be eventually manufactured, and from there to the

field where they have to be used. In this way gas weapons will be better made and better used. The results given by gas have to be known as soon and as completely as possible by the people who establish the gas weapon. Therefore, the organization will be very much the same as the organization of an industry. The director of a great industry has to know what kind of a supply is wanted abroad; then he asks his research branch to find out the best means of making it; then he manufactures the goods; then he sends them out together with travelers to teach the way to use them and bring back information on the results. Thus he will be able to improve upon the methods of, and overcome, his competitors. What I have said for gas weapons may be said for means of protection. Knowing against what kind of gas we have to guard our troops, our chemists have to find out the best respirator, our manufacturers to issue them in large quantities under chemical control, then the men have to be trained before they go up to the line. All information has to be sent back to allow the chemists to improve the means of protection.

The third point is that everything must be arranged to avoid waste of time and effort. By actual collaboration British and French gas services have obtained very good results in this way. By joining in this same collaboration, the United States will be able to start earlier in gas warfare and to afford more quickly good protection for their troops. French laboratories will be only too pleased to take up any research for the American Army and give room to any American workers who may wish to study the subject. French officers of the gas service will be only too pleased to give all information and all directions even on the field to their younger allies.

5. *Plan of organization.*—From the points stated above, the conclusion may be drawn that no sharp division must be made between the offensive and defensive branches; nor between gas service at home and in the field.

The direction of gas service ought to include:

(1) Research department:

- (a) Chemists.
- (b) Physiologists and medical men.
- (c) Manufacturers.
- (d) Gunners.
- (e) Pioneers.

(2) Manufacturing department:

- (a) Schools for special brigade.
- (b) Schools for gas officers.
- (c) Schools for artillery officers.
- (d) Schools for all others.
- (e) Schools for doctors and nurses.

In this way all officers will be trained in the use of gas and means of protection. Special training has to be given to gas officers who are chemists and who will serve the army in this capacity (e. g., chemical advisers of the British Army).

In the Army, besides the special brigade for using cylinder gas and special gas weapons, gas officers or chemical advisers will be attached to each high staff and have the responsibility of planning gas attacks, protection against gas, and the collection of information. Gas officers ought to be attached to "Bureau des Operations, Bureau des Renseignements," and "Service de Sante." They have the supervision of means of protection in regiments and lower units, where instruction, training, and inspection are under the responsibility of all troop officers, who will not be allowed to go into the field without being specially trained in gas schools.

The gas officers belong to the Army, but at the same time they remain in permanent touch with the director of gas service, who gives them all technical directions. A special gas service will be established in France to make the liaison closer with the United States and the American Army as well as with the French and British gas services. All scientific, industrial, and military results will be exchanged between the three above-mentioned allies.

(Signed) CH. FLANDIN.

JULY 30, 1917.

GAS AND FLAME SERVICE, OFFENSIVE AND DEFENSIVE (STATEMENT OF ACTION TAKEN)^a

HEADQUARTERS, AMERICAN EXPEDITIONARY FORCES,

OFFICE OF THE CHIEF OF STAFF,

OPERATIONS SECTION,

Paris, France, July 30, 1917.

Memorandum for the Chief of Staff:

Subject: Gas and flame service, offensive and defensive.

I. *Statement of action taken to date.*—(a) Board of officers convened on June 18, 1917, at these headquarters to investigate questions relating to this subject and to recommend a gas organization.

This board's recommendations were:

1. Assignment of a competent officer to create and handle our gas organization.

2. Pending arrival of such officer (if to come from the United States) the detail of an officer to arrange for supply from the Allies of material, information, and training for our first troops.

3. Provision of ample assistants, funds, and authority to go ahead with this work.

The board made no recommendations as to organization.

(b) On June 25, 1917, the commander in chief cabled The Adjutant General of the Army (cable sent, No. 16, par. 6) requesting authority to retain Dr. G. A. Hulett for gas work and also that either Lieut. Col. James A. Woodruff or Col. Henry Jervy, Engineer Corps, be sent to France to organize gas service under the chief engineer officer.

(c) In General Orders, No. 8, c. s., July 5, 1917, these headquarters, the gas and liquid fire service is placed in the hands of the chief Engineer officer, these headquarters, and the defense gas service is placed in the hands of the chief surgeon, in consultation with the director of gas service.

(d) In the project for the organization of an army, prepared by this section, approved by the commander in chief and forwarded to the War Department, a gas and flame service is provided for in the army troops and one regiment of Engineers is designated for the service.

(e) In the War Department cablegram No. 31, dated July 13, 1917, decision is rendered on the following points:

1. Ordnance Department will provide gas shell.

2. Medical Department charged with defensive measures against gas and to supply gas masks.

3. Gas laboratory established in United States.

4. Nineteen thousand, nine hundred and sixty gas masks shipped July 13, 1917, to France; others to follow.

5. Sanitary section of Medical Department to be established for chemists.

6. Specially selected chemists to be sent to France soon.

7. Gas schools to be established in United States.

8. Reserve mask of French type being manufactured in United States.

9. Masks to be sent with troops.

10. A medical officer, expeditionary headquarters staff, should be designated to keep chief of staff informed of the needs of the gas service, etc.

(f) On July 26, 1917, Maj. J. R. Church, Medical Corps, submitted a study on the organization of a gas service.

The salient points of this study are:

1. Establishment of two gas services; i. e., one in France and one in the United States.

The latter to be subordinate in questions of policy, equipment, etc., to the service in France.

2. The gas service to be independent of any existing arm or staff department in our Army.

3. The service in France to be complete in its independence down to include the officers on division staffs, there be detailed in regiments, battalions, and companies, certain officers and noncommissioned officers with gas service duties, etc.

^a Appendix No. 2, History of Chemical Warfare Service, American Expeditionary Forces, Vol. I, 81.

4. A gas service brigade under the direct control of the chief of gas service, who is to be a brigadier general.

5. The chief of the service to have a staff, laboratories, and meteorological service, and the gas service staff officer on all staffs to be a member of the operations section.

6. Statement made that study, etc., is based on English and French system.

7. A blue print attached to study graphically explains the system.

(g) As far as can be learned from the chief surgeon and chief quartermaster officers the masks sent from the United States have not arrived in France.

(h) The commander, 1st Division, has made urgent requests for masks, claiming the need therefor, but none has been supplied.

(i) Gas schools have been prescribed for the 1st Division.

(j) Cable sent to Adjutant General of the Army, July 29, 1917, requesting officer be designated to commander Engineer regiment designated for gas service and be sent here at once. Colonels Woodruff or Jervy suggested.

II. *Action taken.*—As far as can be learned, the only definite action producing results that has been taken is that indicated in the War Department cablegram. This relates to the United States, except for shipment of masks to France.

It is evident that only a partial solution to this problem has been effected; i. e., adoption of a gas mask and the establishment of schools in the United States and France. Nothing seems to have been actually accomplished on the lines of creating an organization in France.

III. *Requirements.*—Steps should be taken at once as follows:

(a) War Department to establish at home a complete flame as well as gas, offensive and defensive, service.

(b) Decision should be made at once as to whether the material for the gas and flame service is to be supplied from the United States or secured in France.

(c) Steps taken at once to inaugurate a gas and flame service in France in accordance with existing orders and policies of these headquarters. Defensive gas service is our immediate need—it should be developed at once. The fact that the officer to have permanent charge of the whole service is not available should not be a bar to the establishment of the branches of the service. These are needed, especially the defensive branch.

(d) Masks should be furnished the 1st Division without delay by the Medical Department for training purposes, if not for protection.

IV. *Discussion.*—A study has been made of the British, French, and German systems and also that submitted by Major Church, M. C. Consultation has been had with Doctor Hulett, Major Church, and Captain Boothby. These agree with the organization plan submitted. The recommendations and conclusions included herein are the result of the foregoing. It is not deemed advisable to copy or adopt in toto any of the allied systems, but to utilize what appears best for our organization and characteristics.

A chemical service independent and absolutely separate from our established arms and staff departments is not considered necessary nor desirable. Whereas the service should be complete within its organization, it is believed best to make it up from personnel of the Engineer and Medical Corps, which by War Department orders are to furnish the material, etc.

The details of the service and organization for the United States are not considered herein.

The scheme of organization recommended contemplates the use of the Engineer regiment provided for in our army organization project for the offensive service and Medical Corps personnel for the defensive service. At the same time these two services are coordinated by placing the whole service under the commander of the Engineer regiment.

V. *Recommendations.*—(a) Adoption of the organization indicated in and publication of the general order attached.

(b) Upon adoption of the organization indicated the chief surgeon be called upon to designate a medical officer of his corps to take charge of the defensive service. This officer should secure without delay the material and personnel for his branch of the service. He should prepare and publish instructions for all troops and also prescribe the course for all divisional, etc., schools.

(c) While waiting for the commander of the Engineer Gas and flame Service regiment to arrive in France the chief Engineer officer should detail an officer of his corps to start the chemical organization and advance it as much as possible. This work should be done in conjunction with the medical officer in charge of the defensive branch.

(d) If foregoing recommendations are approved, necessary instructions will be prepared.

(Signed) J. MCA. PALMER,

Lieutenant Colonel, General Staff, Chief of Section.

INTER-ALLIED GAS CONFERENCES^a

PROGRAM OF INTER-ALLIED GAS CONFERENCE, PARIS, SEPTEMBER 17-19, 1917

PHYSIOLOGY

1. Discussion of the methods used for the determination of the offensive value of various substances and their adaptability to military use.

- (a) Estimation of toxicity in general.
- (b) Estimation of intensity of suffocating gases.
- (c) Estimation of intensity and penetration of poisonous gases.

2. Discussion of the measures which should in the future serve as a guide in the physiological study of the offensive material.

(a) Discussion of the characteristics of the most importance which each new substance of this character ought to possess and of the relative importance of them.

(b) The permeability of the enemy mask, either through the tissue of the mask or through the box.

- (c) Lessening of protection by the lowering of the absorbing power of the charcoal.
- (d) Insidiousness of gas as a factor.
- (e) Persistence of gas as a factor.

(f) Action of substances either on the protective apparatus or on tissue which is not protected.

3. Discussion on the various results produced by the new gas used by the enemy (dichlorethylsulphide).

- (a) General toxicity.
- (b) Effect on the lungs.
- (c) Cutaneous lesions.
- (d) Relation of the different symptoms.
- (e) Respective intensity of the different actions.

INDIVIDUAL PROTECTION

1. Protection of the parts of the body not covered by the mask against the action of dichlorethylsulphide.

(a) Protection by special clothing of an impermeable nature; different agents which can be used to make clothing impermeable to this gas.

- (b) Disinfection of the clothing and other objects affected by the gas.
- (c) Cleansing of the skin after affection by the gas.

2. The methods of determining the absorbent value of charcoal.

(a) The different systems and their advantages and disadvantages.

3. The question of the protection of the horse.

(a) What must be the protective power of the apparatus:

- 1. During rest.
- 2. During work.

(b) Demonstration of the method of studying the question of horse protection.

COLLECTIVE PROTECTION

1. Collective protection against dichlorethylsulphide.

- (a) The problem of its detection.
- (b) The problem of the protection of dugouts.
- (c) The problem of neutralizing the liquid on or in the ground.

2. Protection of large dugouts.

(a) Supply of pure filtered air for large dugouts.

^a Appendices Nos. 11, 35, 64, History of Chemical Warfare Service, American Expeditionary Forces, Vol. I, 113, 193, 307, respectively. Copy on file, Historical Division, Army War College.

THERAPEUTIC AND CLINICAL

1. The clinical phenomena observed in those poisoned by dichlorethylsulphide.
 - (a) Relative importance of various symptoms.
 - (b) Variation of the importance of different symptoms in accordance with atmospheric conditions.
 - (c) Nature, cause, and frequency of delayed symptoms.
 - (d) Existence of heart symptoms and their significance as to prognosis.
 - (e) Determination as to the cause of the symptoms, whether due to the liquid or the vapor.
 - (f) Nature and seriousness of symptoms in horses.
2. Remedies employed in the treatment of those gassed with dichlorethylsulphide.
3. The employment of oxygen inhalations.
 - (a) Its value in poisoning by suffocating gases.
 - (b) Its value in poisoning by CO.
 - (c) The different methods of administering oxygen, with reference to place (first-aid posts, ambulances, etc.).

The method which was followed was to have the subject under consideration presented by one of the delegates, after which there was a general discussion by those present.

(Signed)

JAMES ROBB CHURCH,

Lieutenant Colonel, M. C.

PROGRAM OF THE SECOND INTERNATIONAL CONFERENCE ON GAS WARFARE, PARIS, MARCH 1-5,
1918

PHYSIOLOGY

First session (9.30 a. m. March 1)

The physiological properties of substances employed by the enemy.

- I. Substances formerly used.
- II. New mixtures.
- III. New fillings.
- IV. New substances.

Physiological action observed in the field and in the laboratory.

The condition of the blood during gas poisoning.

Second session (2.30 p. m. March 1)

Methods of measuring the physiological activity of various products.

The use of volatile anesthetics for the respiratory membrane in the event of penetration of the mask.

Third session (9.15 a. m. March 2)

The physiological properties of the principal series of substances studied in France since the last conference.

CHEMISTRY

The permeability of the German mask.

The use of chemicals in shell and bombs.

Fourth session (2.30 p. m. March 2)

The manufacture and the properties of various aggressive substances.

The preparation and properties of various arsenic compounds, especially of monophenyldichlorarsine.

The preparation and stabilization of acrolein.

Fifth session (9.30 a. m. March 3)

The preparation and stabilization of acrolein (continued).

The use of toxic or irritant smokes.

The preparation of bromacetone.

The preparation and properties of phenylbromacetone.

The preparation and properties of cyanogen chloride.

PROTECTION

Sixth session (2.30 p. m. March 3)

A new protective apparatus in use in the French Army: The A. R. S. mask.

On the degree of protection made necessary by the enemy use of phosgene in projectors.

Protection against particulate clouds.

The protection of the hands and body against dichlorethylsulphide by means of special clothing.

The removal of dichlorethylsulphide from clothing.

Seventh session (9.30 a. m. March 4)

Feeding tubes for masks.

A respirator for individual protection against carbon monoxide.

The protection of dugouts against gas; ventilation.

On the possibility of employing a single neutralizing solution.

THERAPEUTICS

Eighth session (2.30 p. m. March 4)

Chronic symptoms of gas poisoning.

Diphenylechlorarsine poisoning.

The after effects of gas poisoning.

The efficacy of oxygen treatment in cases of gas poisoning.

The medical treatment of gas poisoning.

Ninth session (9.30 a. m. March 5)

The therapeutic value of atropine, digitalin, calcium chloride, etc.

Personal observations on the symptomatology and therapeutics of dichlorethylsulphide cases.

The application, at the front, of Professor Wolf's method for the treatment of gassed cases.

PROGRAM OF THE THIRD INTERALLIED CONFERENCE ON GAS WARFARE, PARIS, OCTOBER 25-30, 1918

THE ORGANIZATION OF ALLIED GAS SERVICES

First session (3.30 p. m. October 25)

Speech by General Ozil.

Interallied relations since March 1, 1918, and the work of the permanent interallied secretariats.

The collection and classification of documents.

The present status of chemical services in America.

PRODUCTS EMPLOYED BY THE ENEMY

Second session (9.30 a. m., October 26)

Enemy use of gas on the British front since March, 1918.

Products employed by the enemy since March 1, 1918; a variation in yellow cross shell fillings.

The physiological properties of substances used by the enemy.

Toxicological examination of the viscera of gas casualties.

Third session (2.30 p. m., October 26)

The general nature of cases of yperite poisoning in the British forces.

Blood pressure in yperite poisoning.

Modifications in the blood during yperite poisoning.

Histological observations made in fatal cases of yperite poisoning.
 On the effects produced in the field by chlorarsine compounds contained in blue ~~cross~~ and yellow cross I. shell.
 The pathology of phosgene poisoning.
 Lesions occurring on horses exposed to gas—particularly yperite.

PROTECTION

Fourth session (9 a. m., October 27)

The detection of yperite in the air, on the ground, and in water.
 A method for the detection of yperite on the ground and in the air; the use of yperite detectors.
 The value of the protection given by the A. R. S. mask.
 The military value of the A. R. S. mask; the length of time that it can be worn.
 The production and properties of better charcoals for respirators.
 A comparison of the activity equations of the new German charcoal and the allied charcoals.
 The French charcoal.
 The protection of horses.

Fifth session (2.30 p. m., October 27)

Defense against yperite.
 Protection against yperite.
 Means for protecting the skin against yperite; the possibility of their use in the field.
 Disinfection of objects contaminated by yperite.
 Ventilators and filtering apparatus for dugouts.
 Protection against carbon monoxide during firing.
 The protection of tank crews.

PHYSIOLOGY

Sixth session (9 a. m., October 28)

The action of lacrymators and vesicants on the eye.
 Specific sensibility to vesicants.
 The measurements of vesicant power.
 The transformation of yperite within the organism; the physiological action of its disintegration products.
 A study of new substances prepared for offensive use.
 The secretion of arsenic by animals gassed with ethyldichlorarsine.

CHEMISTRY

Seventh session (2.30 p. m., October 28)

Physical constants of certain gases used in chemical warfare.
 Gas camouflage from the laboratory point of view.
 The production of particulate clouds by bombs or shell.
 The pulverization of special liquids.
 Experimental work.
 The motion of a liquid-filled projectile.
 Recent work on yperite.
 The quantitative determination of yperite.
 The action of different oxidizing agents on yperite.

Eighth session (9 a. m., October 29)

The physicochemical properties of solutions of yperite in various solvents.
 The physiological properties of solutions of yperite in various solvents.
 Progress achieved in France in the manufacture of yperite.
 The use of phenyldichlorarsine as an offensive substance.
 The preparation of phenyldichlorarsine.
 Researches on the arsine series.
 Progress achieved in France in the manufacture of arsines.

Ninth session (2.30 p. m., October 29)

The quantitative determination of diphenylchlorarsine and of diphenylamine—chlorarsine in particulate and vapor form, and its relation to penetration of the German mask.

The alcoholization of arsines.

On cyanogen compounds, the use of cyanogen chloride and bromide

Orthonitrobenzylbromide.

Homomartonite and semimartonite.

Details on the manufacture of comite.

Carbon monoxide as an offensive substance in chemical warfare.

The permeability of the German mask; protection given by the new German respirator.

THERAPEUTICS

Tenth session (9 a. m., October 30)

Demonstration of a portable apparatus for the administration of oxygen.

Demonstration of apparatus used for the administration of oxygen in the French army.

The administration of oxygen in cases of gas poisoning.

The physiology of oxygen treatment and blood letting in cases of gas poisoning.

The therapeutic effect of blood letting, and of the injection of an isotonic, saline solution in animals gassed with lethal concentrations of chlorine, chlorpierin, and phosgene.

The treatment of phosgene poisoning.

The dangers of general anesthesia in gassed men.

Respiratory exercises as treatment for the pulmonary after-effects of gas poisoning.

The treatment of yperite burns.

Therapeutic materials in use in the French army.

THE PHYSIOLOGICAL EFFECT OF WARFARE GASES ON THE HUMAN BEING INCLUDING SYMPTOMATOLOGY, PATHOLOGY, AND GENERAL TREATMENT *

[Compiled by medical adviser of the chief of Gas Service, A. E. F.]

FEBRUARY 8, 1918.

The employment by the enemy of poisonous gases as a means of offensive warfare makes it imperative that all medical officers should have some knowledge of the actions of the important gases used and of the rational lines of treatment which may be adopted in cases of gas poisoning. To that end the following notes are offered. It must be thoroughly understood that the enemy is constantly introducing new gases or combinations of gases, and that new conditions may arise which will make it necessary to modify many of the statements herein published.

With few exceptions the general symptoms of all asphyxiating gases are similar; so much so that these symptoms will be enumerated as a whole.

Mustard gas, however, presents so many different phases of the subject that it will be treated separately. There are also a few differences between the physiological effects of chlorine and phosgene.

Phosgene upon meeting moist surfaces is broken up, and hydrochloric acid liberated. It excites less spasm in the upper respiratory tract, thereby making it possible to penetrate to the innermost recesses of the lungs, where it causes an irritant edema, which may be, and often is, delayed an hour or more in its action. There is also much greater tendency to circulatory failure and the features suggestive of general collapse are more in evidence. Mustard gas produces serious burns due to direct contact with the gas. The most dangerous burns encountered are those of the respiratory path; these differ from the burns of phosgene in that they are in the upper respiratory passages. Most patients suffering from mustard-gas poisoning are subject to secondary infection. There is never present the enormous effusion of serum occurring in phosgene.

There is no fundamental difference between the effect of gas shells and that of cloud gas, though there may be slight differences owing to attendant circumstances. Due to higher concentrations, the deaths from phosgene and chlorine clouds are about four times as much as from the same gases from artillery shell.

All gases are capable of producing multiple symptoms. On the one hand, there is the immediate irritant, corrosive, and poisonous action of the gases; on the other, the remote effects due to the disturbance of gaseous exchange and secondary infections which are favored by the damage to the respiratory organs and to the specific toxic action due to the disorganization of the tissue elements in consequence of the corrosion.

The degree of the symptoms produced depends upon (1) the concentration of the gases, (2) duration of its action, (3) the effectiveness of the protective contrivances (respirators, masks, etc.) and the method of their employment.

The natural resistance of the soldier and his general health must also be carefully considered in connection with these cases. No hasty conclusions must be drawn from first observations of the patient for the reason that the action of the concentrated gas for a short period may cause the most intense corrosion though but small amounts of the poison may have been absorbed in the blood; again large amounts of the poison may have been absorbed in the blood with but little evidence of corrosiveness. Again mild cases of poisoning can be readily transformed into the gravest symptoms as a result of bodily activity, foul, dirty air, or as a consequence of the onset of secondary infection.

In treating cases suffering from gas poisoning the following must be carefully considered: Actions of the gas or vapors on—

1. The skin.
2. The eyes.
3. The mucous membrane of the air passages and tissues of the lungs.
4. The blood and the circulatory organs.
5. The nervous system.
6. The digestive organs.
7. The urinary organs.

* Copy on file, Historical Division, S. G. O.

As a rule, the first place in which the violent action of the gas is evident is in the air passages and in the alveoli of the lungs. The irritation is immediately followed by an inflammatory reaction characterized by congestion, by swelling of the mucous membrane, and by increased secretions in the air tubes, edema, and inflammatory formations.

With nearly all gases there can be expected attacks of coughing and burning pain in the chest, a feeling of pressure and breathlessness, which may come on at once or which may often be delayed for several hours according to the kind and concentration of the gas. In slight cases the symptoms may be limited to these and disappear during the course of 24 hours. In the more severe cases the distress becomes intolerable. The patients wail, groan, struggle for air, and toss themselves restlessly about. Their color varies from bluish red to the deepest cyanosis; breathing rapid and shallow, and becomes in the later stages irregular and faltering. The initial dry coughing soon begins to furnish a copious sputum, thin, fluid in character, albuminous, frothy, and often blood stained. There may be marked emphysema of the lungs, crackling râles, and diminished breath sounds. The body temperature rises from 102° to 105°, which generally occurs on the second and third days, accompanied by signs of bronchopneumonia of a greater or less severity. The breathlessness and cyanosis become more intense, and signs of resonating and crepitant râles can be found scattered throughout the lungs.

As a rule, however, the bronchopneumonia which appears during the first day or two and which seems to be due directly to the action of the gas and not to bacterial infection does not prove fatal save in a few cases. The symptoms usually disappear with a fall in temperature after a few days; usually, in fact, after two or three days. Those due to the action of harmful warfare gases on the lungs are considerably influenced by disturbances of the circulation, which are apparently caused by the diminished supply of oxygen to the blood.

DIGESTIVE APPARATUS

Gassed cases complain very frequently from the beginning onward of loss of appetite pain in the stomach, malaise, and nausea. Frequently the pain in the region of the stomach may last several days following recovery from gas poisoning. Diarrhea, with occasionally blood in the stools, is less frequent.

CIRCULATION

The ordinary phenomena in asphyxia of mechanical origin is that the blood pressure rises and that the heart soon loses its full driving power because its muscle can not maintain this increased effort when it is working with a scanty supply of oxygen. Consequently the pulse rate quickens, the right heart dilates, and the blood tends to pool up behind it in the veins. If this failure proceeds apace, a patient who at the beginning showed congestive cyanosis of the face, with a full pulse, will gradually assume a gray pallor, while the pulse accelerates and falls off in power. These changes are augmented by the edema of the lungs, which directly obstructs the pulmonary circulation and causes an earlier failure of the right heart.

If the patient during this critical period tries to perform his work, he will use up still more rapidly the little oxygen that he is receiving, extra work will be loaded onto a heart which is already overstrained, and the circulation will be likely to fail still more speedily on account of the difficulty of maintaining compensation in the upright position.

URINARY ORGANS

In general no symptoms are shown in the urinary organs. Occasional cases of difficulty of urination or of retention of urine are found, but these may be attributed to nervous influence. The quantity of urine is not materially altered, while the color generally remains normal.

PROGNOSIS

A prognosis can only be made with the greatest caution in the first few hours. The majority of cases may be grouped straight away into classes: Mild, moderately severe, and severe. As a rule the quite trivial cases and the quite hopeless cases may be quickly recognized. It must not, however, be forgotten that cases which appear slight may suddenly develop very severe symptoms, and cases that exhibit the most profound asphyxial symptoms or the deepest unconsciousness may, after the lapse of only a few hours, give the impression of being out of danger. In these later cases, as a rule, the improvement is but transitory.

DIAGNOSIS OF MUSTARD GAS CASES

It is not necessary to spend much time on the diagnosis of these erythemas, bullae, or even upper pharyngo-laryngeal disturbances, which are sufficiently typical to be recognized without any definite etiological information.

When the burns are limited to the face or the arms, one may think of the uncharacteristic burns due to a jet of liquid fire or some explosive. But in this latter case the lesions are very much deeper and the pain much more accentuated.

There should be no difficulty in recognizing the erythema; but perhaps the erythema of the eyelids, bullous or not, might be taken for an intense erysipelas; or the erythema of the back and extremities for a scarletina or prevariola rash, but the fever is absent. On the other hand, if limited to the face there is no glandular involvement; if limited to the extremities, even though most marked on the flexuous surfaces, there is no red mottling and it is smooth to the touch, with scattered white spots or minute droplets, like bullae, visible only in a tangent light.

A study of the eosinophilia of the blood may be of real importance. If it occurs in erysipelas or in scarletina, it is late and not marked. On the contrary, it occurs early in toxic erythema (Loeper).

One of the important points of this poisoning is its resemblance to certain artificial dermatites, due to the criminal appliance of different caustics. The alkalis make soft, the acids hard, eschars, which are single or few in number, darker in color or very much deeper than the lesions produced by these gases. The lesions produced by croton oil are somewhat analogous; also those produced by the essence of mustard, the nature of which perhaps is not very different. Apart from the limitation of the process in the cases of malingering and its extent in the intoxications, which we are considering, there is no sure means of diagnosis, the more in so much as eosinophilia exists in both cases.

The first isolated cases of burns which were seen in French hospitals, chiefly the ones who had a well-limited and almost rectangular phlyctene, might have been, and perhaps were, considered as cases of voluntary mutilation, and the blister may have been taken for a cantharides blister.

Finally, the pigmentation, so characteristic, described above, gives a most important means of diagnosis, for we do not know of any so intense, so extensive, so constant, so deep in color in the dermatites.

POST-MORTEM FINDINGS FROM CHLORINE AND PHOSGENE

In a case of death at 24 hours after gas poisoning, the trachea and bronchi are purple red and congested, while a thin exudate wells up into them from the lungs. The latter organs are heavy and edematous, while areated islets of emphysematous over distension alternate with depressed purple patches of collapse. On section, serous fluid drips abundantly from the lung tissue. Air that has escaped from ruptured vesicles is seen in chains of bubbles on the surface of the lungs, along the interlobar fissure, and even penetrating the tissue of the mediastinum. In some of the earliest cases the most intense disruptive emphysema may be observed, destroying the air sacs and interfering with the circulation of their walls.

Petechial hemorrhages appear on the surface of the lungs, on the heart, and also on the inner surface of the stomach. All the veins are greatly distended and the abdominal viscera are engorged with dark blood that clots very early after death. The heart itself may fail to show right-sided dilatation, for this does not of necessity appear post-mortem in cases of asphyxial death.

If the man succumbs at a later date, inflammatory complications appear in the lungs. There is superficial pleurisy, scattered bronchopneumonia, and a purulent secretion in the bronchi. The serous exudate will then be found to have disappeared and no fluid drops from the cut surfaces of the lungs.

POST-MORTEM FINDINGS FROM MUSTARD-GAS POISONING

Skin lesions.—Usually very superficial and do not involve the deeper layers.

Mouth and throat.—The mucous membrane shows various stages of an acute inflammatory process, from a simple reddening to swelling, excretion, ulceration, and sloughing of the membrane. The larynx is usually severely affected and the cords may be ulcerated. Large sloughs are common.

Thorax.—Pleural effusions of moderate degree have been reported, but are not the rule.

Lungs.—Cases dying within the first six days frequently show marked pulmonary edema, with superficial hemorrhages and emphysema. Areas of septic destruction of the lung tissue may be found.

Pericardium.—Occasionally contain a small amount of clear serous fluid.

Heart.—Tough and firm ante-mortem clots sometimes found, especially in right auricle and extending to large vessels and right auricle. Myocardium, as a rule, appears normal.

Abdomen.—Stomach may show zones of acute congestion and sometimes submucous hemorrhages. Intestines similar changes as stomach.

Liver.—Signs of fatty infiltration; organ enlarged.

Spleen.—Nothing.

Kidneys.—Capsule strips easily; may be fatty.

Brain.—May show signs of congestion.

Blood.—Increase in its coagulability reported.

TREATMENT

General considerations.—In discussing the general treatment of gas poisoning in warfare, several things must be considered: The nature of gases used; the manifold symptoms and varying severity of different cases; and the place where treatment is to be administered, whether in the trench, dugout, field ambulance, evacuation, base, or general hospitals. It must also be remembered that, on the one hand, there is the immediate irritant, corrosive, and poisonous actions of gases, and that, on the other, there are things consequent with disturbance of gaseous exchange as well as on secondary infections which are favored by the damage to the tissues of the respiratory organs. The specific toxic action of disorganized tissue must also be considered.

As a rule, however, whenever much definite discomfort or grave symptoms are evident, the principles of treatment are as follows:

1. To diminish the respiratory activity of all gassed cases so far as possible.
2. To improve the supply of oxygen.
3. To combat the pulmonary edema and inflammatory changes in the lungs.
4. To keep the circulation going.
5. To promote the excretions of poison from the body.
6. To prevent the onset of secondary infections.
7. To alleviate the pain and discomfort.
8. To keep the patient warm.

Rest.—(1) Respiratory activity of the organisms depends mainly on the degree of muscular activity. The greatest care must therefore be taken to prevent any muscular exertion in all cases. Such cases must not be allowed to walk, either alone or with assistance, but should be carried on stretchers whenever possible. All equipment that hinders the play of the respiratory muscles, such as belts, braces, etc., will be removed.

(2) There is obviously no treatment that can be directed against the effects of the chemical on the respiratory membrane. The only effective treatment thus far recognized is—

First. To diminish the amount of blood serum available for this effusion, which is done by bleeding, and by restricting the intake of water. Bleeding is done at the very earliest opportunity, and 2 pints of blood removed as rapidly as possible.

Second. To give oxygen in high concentration. This is most economically and comfortably done by a catheter in the nose, which delivers oxygen in the nose pharynx. The subcutaneous injection of O is useless.

Third. To place the patient with head lower than feet to aid in draining the serum that accumulated in the trachea and large bronchi.

Fourth. To produce artificial respiration if necessary.

Special stimulants and drugs.—Ammonia is very useful as an inhalation, but in using this drug care must be exercised not to apply its fumes too near the face. It should be discontinued as soon as labored respiration is noticeable.

Atropine has been used extensively by the British and French, with a view to checking the secretion of fluid.

Digitalin, $\frac{1}{16}$ grain, hypodermically, has been used to some extent, but not very successfully.

Morphia, $\frac{1}{2}$ grain, is most useful as a sedative.

Strychnine, $\frac{1}{4}$ grain, has been used in later stages of collapse.

TREATMENT FOR MUSTARD-GAS POISONING

In view of the special characteristics of mustard-gas poisoning, the following additional notes are given relative to the treatment of these cases.

Before discussing this subject, however, it might be well to review briefly some of the symptoms and special characteristics of this important gas.

The principal effects of poisoning from mustard gas may be summed up as follows:

First. Irritation and vesication of the skin and mucous membranes, conjunctival, laryngeal, pharyngeal, etc., which are caused for the most part by the actions of the acid vapor.

Second. Bronchopulmonary complications, which seem to result from secondary complications.

Third. The importance that soiled clothing plays in relation to this poison.

In considering the treatment for this poison, each of the above must be carefully considered and studied.

From our knowledge of the clinging properties of this gas to clothing, it can be seen that prior to administering treatment of any kind the infected clothing must first be removed and gotten rid of. Next the body must be cleaned. This is best done as follows: Sponge the entire body, including scalp, with warm water, soap, and brush, bicarbonate of soda 20 per 1,000, or lime water 1 per 1,000. After drying, the patient should be issued clean clothing. The infected clothing should be soaked in bicarbonate of soda solution for a half hour, rinsed in clean water, and hung out to dry.

All persons coming in contact with mustard-gas cases should have their hands protected with gloves, and as an extra precaution, must bathe all exposed surfaces with bicarbonate of soda solution at the conclusion of their duties.

When possible a special building or tent should be used for the first treatment of these cases, thus avoiding infecting others.

Treatment of the eyes.—Wash the conjunctiva with a solution of bicarbonate of soda 1 per cent strength, then treat them with a little sterile oil. In washing the eyes use a syringe or douche cup, opening the eyelids wide, inverting them if possible, and paying particular attention to the condition of the corners. This treatment should be administered several times daily. In milder cases the most troublesome complication is usually the photophobia resulting from burns of the eyes, and the only treatment in these cases is protection against the light.

Treatment of mucous membranes.—The nasal and pharyngeal mucous membranes should be thoroughly cleansed with bicarbonate solution. In severe cases, with persistent cough due to ulcers of the trachea, the condition is best treated by steam inhalations and cough mixtures.

Gastrointestinal complications.—Regulation of the diet is of the utmost importance—a milk diet or, if necessary, plain water diet. The internal administration of 20 grains of bicarbonate of soda is often beneficial.

Respiratory symptoms.—Eucalyptus inhalations and fumigations should be used early, relieving the patients; acting as antiseptics, they appear to prevent secondary infections which affect the respiratory system.

Gas respirator.—To prevent air-borne infections, the wearing of a respiratory mask made from aluminum, perforated, and made to fit over the mouth and nose and retained in place by means of small strings in which is placed absorbent cotton saturated with the following solution:

R Menthol	40 grains.
Chloroform.....	
Creosote.....aa	2 drams.
Tr. iodi.....	1 dram.
Sp. vini rect. qs. ad.....	2 ounces.

M. Fifteen drops on wool of mask every hour.

Cutaneous symptoms.—Blisters should be pricked with antiseptic precautions. The following dusting powder will be beneficial:

R Talcum powder.....	400 grams.
Carbonate of lime.....	
Carbonate of magnesia.....	
Oxide of zinc.....aa	200 grams.

Dust freely over parts and cover with a nonabsorbent wool. Compresses soaked in limewater may also be used. The main object in view is the neutralization of the gas, and the sooner this is accomplished the better will be the patient's chance of early recovery.

NOTE.—At present efforts are being made to neutralize the effects of the gas by giving intravenous injections of hexamine (urotropin), which looks very favorable.

H. L. GILCHRIST,
Lieutenant Colonel, Medical Corps, U. S. Army.

THE 28TH DIVISION

HEADQUARTERS FIELD HOSPITAL COMPANY NO. 110,
OFFICE DIVISION MEDICAL GAS OFFICER,
28TH DIVISION, A. E. F.,
September 1, 1918.

REPORT OF GAS CASUALTIES FROM AUGUST 5 TO AUGUST 31, 1918

1. In submitting this report of gas casualties admitted to this hospital from its opening on August 5 to August 31, 1918, I desire to invite your attention to the attached scheme, which will, I believe, readily give all information concerning cases admitted from the 28th Division, as well as all other divisions represented in the casualties.

2. By referring to the scheme, it can readily be determined, for instance, how many casualties were admitted from Company D, 109th Infantry, by reason of:^b

(1) Allied gasses (phosgene, chlorine, chloropierin, and the chlorarsine compounds); (2) mustard gas; (3) evacuations; (4) returned to duty; (5) totals, both per company and regimental.

3. It will be noted that casualties were admitted from a number of divisions other than the 28th and are included in the report; also that the following order of entry is carried out: (1) Infantry; (2) Artillery; (3) machine gun battalions; (4) Engineers; (5) military police; (6) field signal battalions; (7) Medical Department; (8) American Red Cross; (9) anti-aircraft machine gun battalions; (10) French.

4. So far as is known, no new gasses were used by the enemy during the recent operations, and we can only attribute the large number of casualties covering this report of 26 days as being due to the fact that many of the men were experiencing their first prolonged exposure to gasses, and not understanding the effects of this type of weapon nor being able to differentiate between a short inhalation of a slight concentration and the slight inhalation of a more concentrated gas; consequently many men, when they first felt the slightest constriction of the chest with some disturbance in breathing and eye involvement, considered themselves gassed and became somewhat panic-stricken. Hence their first instinct was to resort to the hospital for relief; when, instead, a few hours' removal from the gassed areas would have been sufficient to have returned many of them to duty.

5. This in a measure will explain the large number of cases admitted to the hospital and returned to duty after a 24 to 38 hour duration. It must be remembered, however, and consistently considered, that many of these men were in a state of fatigue or on the borderland of exhaustion during the early period of days embodied in this report, and this factor would in a considerable measure have an influence directly encouraging a possible psychic condition.

6. Interrogation of many patients revealed the following causes of casualties: (1) Asleep in dugouts during and following gas bombardments; (2) "gas-clear" alarm sounded and respirators removed too soon; (3) defective and improperly fitting respirators; (4) lying on gassed ground; (5) lying on gassed blankets and in gassed clothing; (6) failure to change clothing after knowledge of having received splash of mustard gas; (7) explosion of gas shells close by and not sufficient warning to adjust respirators; (8) wearing respirators without facepieces on, only mouthpieces and nose clips being used; (9) respirators knocked off during engagement or excitement; (10) failure to adjust respirator; (11) testing for gas by one noncommissioned officer given as cause for his being gassed (eye case).

7. We feel that while gas casualties are bound to occur, there is no doubt many could have been avoided by greater precaution and stricter adherence to gas discipline.

8. During the first 6 days after the opening of the hospital all cases were evacuated after various periods of rest and treatment ranging from 24 to 36 hours. After the first 6 days, severe cases alone were evacuated and the remaining cases were returned to their commands after periods ranging from 12 hours to 5 days in the hospital.

^b Only four organizations are given below, with totals for all, the purpose being merely to show the method employed for reporting casualties.—Ed.

9. By reference to the attached scheme it will readily be noted that the large number of cases returned to their commands; that the measure alone of holding and treating these mild cases has retained for the division a considerable number of its fighting force. Of casualties retained and treated, the following comprises an approximate list: (1) Over 80 mustard-gas burns of first, second, and third degree were returned to duty, cured; (2) approximately 200 eye casualties were returned to duty, cured; (3) approximately 200 slight chest involvement cases were returned to duty, cured; (4) 40 cases of aphonia (loss of voice from laryngeal involvement) returned to duty after 4 to 5 days' treatment; (5) 11 cases of epistaxis (nosebleed) due to mustard-gas inhalation returned to duty; (6) effort syndrome (D. A. H.) 15 cases returned to duty; (7) venesection (bleeding) 17 cases returned to duty, all mustard-gas cases, severe.

10. The average stay in hospital of all cases returned to duty has been three days. A number of aphonic cases were returned to duty before entire return of voice. This was done for a twofold purpose: (1) To overcome a notion in the minds of a number of these cases that their voices would not return, thereby overcoming a possible permanent psychic influence. (2) Since the aphonia is purely functional and not organic, and all physical distress having disappeared, together with the fact that these cases linger in the aphonic state for periods ranging from two to three weeks, it was decided that the man could do duty with his command and thus be of service to the division without any material injury to himself, treatment having but little beneficial effect after the first four or five days, depending upon, of course, the presence or nonpresence of ulceration.

HOWARD C. HARPER,
Captain, Medical Corps, Divisional Medical Gas Officer.

THIRTIETH INFANTRY

	Hdq.	Sup.	M. G. B.	A	B	C	D	E	F	G	H	I	K	L	M	Total
Allied gas.....	0	0	1	0	0	0	0	0	1	1	7	0	0	0	0	10
Mustard gas.....	0	0	0	0	0	0	2	0	0	5	0	0	0	0	0	7
Company total.....	0	0	1	0	0	0	2	0	1	6	7	0	0	0	0	17
Evacuated.....	0	0	1	0	0	0	2	0	1	5	3	0	0	0	0	12
Returned to duty.....	0	0	0	0	0	0	0	0	0	1	4	0	0	0	0	5
Remaining.....	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

THIRTY-SIXTH INFANTRY

	Hdq.	Sup.	M. G. B.	A	B	C	D	E	F	G	H	I	K	L	M	Total
Allied gas.....	1	0	0	2	0	0	0	0	0	1	0	1	3	0	0	8
Mustard gas.....	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	2
Company total.....	1	0	0	2	0	0	0	0	0	1	0	2	3	0	1	10
Evacuated.....	0	0	0	0	0	0	0	0	0	0	0	1	2	0	1	4
Returned to duty.....	1	0	0	2	0	0	0	0	0	1	0	1	1	0	0	6
Remaining.....	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

THIRTY-NINTH INFANTRY

	Hdq.	Sup.	M. G. B.	A	B	C	D	E	F	G	H	I	K	L	M	Total
Allied gas.....	0	2	0	0	0	0	0	3	2	2	0	0	1	1	0	11
Mustard gas.....	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Company total.....	0	2	0	0	0	0	0	3	2	2	0	0	1	1	0	11
Evacuated.....	0	1	0	0	0	0	0	0	0	1	0	0	0	1	0	3
Returned to duty.....	0	1	0	0	0	0	0	3	2	1	0	0	1	0	0	8
Remaining.....	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

FIFTY-EIGHTH INFANTRY

	Hdq.	Sup.	M. G. B.	A	B	C	D	E	F	G	H	I	K	L	M	Total
Allied gas.....	0	0	0	0	0	0	0	0	1	2	0	0	0	0	0	3
Mustard gas.....	0	0	0	1	2	1	0	0	1	2	1	0	0	0	0	8
Company total.....	0	0	0	1	2	1	0	0	2	4	1	0	0	0	0	11
Evacuated.....	0	0	0	1	2	1	0	0	2	3	1	0	0	0	0	10
Returned to duty.....	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1
Remaining.....	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

NOTE.—Other organizations are omitted here.—Ed.

Summary of totals

Total admission.....	1, 422
Evacuated.....	849
Returned to duty.....	550
Remaining.....	23

THE 90TH DIVISION

TRIAGE, 90TH DIVISION, A. E. F.,

France, November 15, 1918.

From: The division medical gas officer.

To: The division surgeon.

Subject: Final report.

1. I am handing herewith a brief summary of the work accomplished in medical gas defense in this division. Also a complete report of gas casualties occurring in the division from August 25, 1918, to November 15, 1918, inclusive.

2. The organization of the medical gas defense in the 90th Division was begun and accomplished amid some difficulties. The work was not undertaken until the division had taken over its sector in the St. Mihiel salient. Only a few medical officers and noncommissioned officers had had the advantage of a course of instruction at the gas school. After having been designated division medical gas officer, organization and instruction of the medical officers and the enlisted personnel of the Medical Department of the division was immediately begun. The division being very short on transportation, and the tables of organization providing none, made it next to impossible to accomplish anything at the outset. There was also great difficulty in obtaining antigas supplies, drugs, oxygen, etc. This difficulty was overcome later by the division medical supply officer, and an ample supply of everything was obtained so that modern treatment was available in every instance. The transportation problem was overcome by the division surgeon detailing his own side car in the beginning and later detailing one exclusively for this work.

Field Hospital No. 358 was designated as the division gas hospital. The officers and enlisted men of this institution were instructed and drilled in degassing and treatment of gas casualties, members of the personnel impersonating patients.

The officers and personnel of the ambulance companies were instructed in the degassing and treatment of gas casualties at the ambulance dressing stations. They were also instructed in the transportation of these cases.

Regimental and battalion surgeons, their enlisted personnel, and litter bearers were instructed in first aid to the gassed. This was all accomplished while the division was holding the sector, and instruction was kept up during and after the drive of September 12 and 13, 1918.

Full and complete instructions covering every conceivable detail in the handling of a gas casualty, from the time he was picked up in the field until he was discharged from the hospital, was published by your office and sent to every medical officer in the division.

It was found that each medical officer was alert to the situation; and after the organization was completed, each mustard case had had eyes, nose, and throat irrigated, armpits and genitals bathed with alkaline solution at the battalion aid station (one battalion surgeon handling over 150 such cases in one day). At the ambulance dressing stations the degassing of these cases was completed, so that on arrival at the division gas hospital practically every mustard-gas case had been degassed.

In order to keep sufficient antigas supplies at the battalion aid stations an antigas kit was devised. An ambulance food box was marked "antigas equipment" and filled with the necessary articles required in administering first aid to the gassed. Each battalion surgeon was issued one of these kits. Each ambulance carried one at all times, and a stock of these kits were kept on hand at the division medical supply depot. Exchanges were made in the usual way.

During the activities on both fronts only two cases were brought to my attention that were not gassed. A second lieutenant who had pulmonary tuberculosis and gave no history of gas; the other a cook who was promptly returned to duty. Not only did we not have gas malingerers in the division but we had many men who fought with their mouthpieces and nose clips adjusted, eyes being exposed (because of fogging of eyepieces), and who later

developed trouble with their eyes, reported to battalion aid stations for treatment and voluntarily returned to duty. Also on one occasion when a battalion suffered more than 150 casualties the remainder of the battalion continued to do duty until relieved from the St. Mihiel salient. On reporting in the Meuse sector the battalion surgeon requested that this battalion be examined to ascertain its fitness for active field service. It was found by a board of medical officers (appointed by the division surgeon) that 3 officers and 130 men had suffered to such an extent that it was necessary to evacuate them from the division. None of these men had reported to the battalion aid station while in the St. Mihiel sector.

The type of gases employed by the enemy varied. He usually employed lacrymators and stenutators well mixed with diphosgene. The division was subjected to two severe mustard-gas bombardments while in the St. Mihiel sector. There were 460 mustard-gas cases as the result of the bombardments. Little mustard was used by the enemy in the Meuse sector, only 59 cases occurring, all of which was by contact and none by inhalation.

Nearly all cases of gas poisoning by inhalation were caused by gas shells bursting near men who were caught unawares without their respirators adjusted or by the men removing their masks because of the fogging of the eyepieces. Many men were gassed during advances when they took refuge in fresh gas shell holes. There were some inhalation cases developed by men being in extremely low concentrations of gas for a long period of time and, not realizing the danger, did not adjust their masks.

In the St. Mihiel sector no case was evacuated from the division until he had been under observation at the gas hospital one week or longer and only when it appeared that it would require weeks for him to recover. Neither was a case sent to duty until he had been up and about 24 hours and tested for "effort syndrome." This resulted in few cases being returned from their command.

The only disaster inflicted by the enemy occurred in the early morning of September 27, 1918, when he secured a direct hit with a diphosgene shell on a dugout in which our men were sleeping. The men were caught unawares and evacuated the place through a valley that had been previously shelled with mustard gas. All these men were, therefore, gassed first by inhalation of diphosgene, and those who were unable to adjust their masks also got mustard by inhalation. All were severely burned. Under the circumstances the men necessarily received heavy concentrations of both gasses. The prompt evacuation of the area and the prompt evacuation of the men to the gas hospital where they received heroic treatment no doubt saved the lives of many. There were 17 fatalities.

A visit to the gas hospital at Toul, and later to La Morlette, revealed the fact that all cases evacuated from the division were of moderate severity. At the time of the visit no deaths had occurred among men from this division.

There was a total of 1,390 gas casualties in the St. Mihiel sector, 844 of which were returned to duty from the division gas hospital, 529 evacuated from the division, and 17 fatalities. There was a total of 785 gas casualties in the Meuse sector, 10 of which were returned to duty from the division gas hospital, and no fatalities, making a grand total of 2,175 gas casualties occurring in the division during all of its activities, 854, or 39.27 per cent, being returned to duty, 1,304, or 59.95 per cent, were evacuated from the division, and 17 fatalities, or 0.78 per cent. The large number of evacuations from the Meuse sector was due to the rapid advance making it impossible to hold cases sufficient length of time in the division gas hospital. The low percentage of fatalities was due to gas discipline, prompt and proper evacuation, early and definitive treatment.

This being the final report from this office, may I not express my appreciation of the whole-hearted cooperation on the part of the division surgeon, all regimental and battalion surgeons, medical officers of all ambulance companies, the division medical supply officer and the officers and men of Field Hospital 358.

(Signed) CHARLES M. HENDRICKS, Major, M. C.

[First indorsement]

HEADQUARTERS 90TH DIVISION, O. D. S.,
AMERICAN EXPEDITIONARY FORCES,
France, November 16, 1918.

To the Chief Surgeon, A. E. F.

(Through commanding general, 90th Division.)

1. Forwarded. Attention invited to the excellent record in the treatment of gas cases in this division. A mortality of only 0.78 per cent of the total cases is the best index of the efficiency of the training of the personnel, both in gas discipline and the intelligent handling of those gassed.

2. I wish to commend the work of Maj. Charles M. Hendricks, M. C., through whose efforts the medical personnel of the division reached a high degree of proficiency in the treatment of gas cases.

P. S. HALLORAN,
Colonel, Medical Corps, Division Surgeon.

REPORT OF CONSULTANT IN GENERAL MEDICINE FOR GAS POISONING

OFFICE OF THE CHIEF CONSULTANT,
MEDICAL SERVICES, AMERICAN EXPEDITIONARY FORCES,
U. S. ARMY, P. O. 731,
France, December 17, 1918.

From: Consultant in general medicine for gas poisoning.

To: Chief consultant, Medical Services, American Expeditionary Forces.

Subject: Report of activities of section of gas poisoning.

1. According to instructions contained in letter from chief surgeon, American Expeditionary Forces, to the director of professional services, American Expeditionary Forces, of November 16, 1918, following report is submitted:

2. The activities of the section of gas poisoning have been as follows:

(a) Instruction.

(b) Treatment and hospitalization.

(c) Actual supervision of the care of the gassed.

3. Instruction was carried out either by circularization or by lecture. Circular No. 34, chief surgeon's office, which had to do with the treatment of gassed patients, was prepared in this office. Other circulars in regard to the treatment of gas poisoning were from time to time prepared in this office. Either the consultant in general medicine, in charge of gas poisoning, or other representatives of this office gave lectures on the subject of the care and hospitalization of the gassed. These lectures were given to medical officers either in divisions or at the Army sanitary school at Langres.

4. The large question of the hospitalization and of treatment of gassed patients, especially in division and army areas, was given much study. An endeavor was made by advice and conference with those in authority to emphasize the important but simple principles involved and to achieve their acceptance throughout the American Expeditionary Forces. After comparatively little study it became obvious that the question of the care of the gassed was largely an administrative one. From the clinical point of view the question is simple. The diagnosis of the two main "gas diseases"—i. e., the "suffocative gas disease" and the "vesicant gas disease"—offers little difficulty. Also the treatment is simple and only calls for the exhibition of a sound knowledge of medicine and of ordinary common sense.

Stress has always been laid by this office on the importance of early bleeding in those poisoned by suffocating gases. From clinical observation it is deemed probable that bleeding is the one most important factor in the successful treatment of these conditions; second in importance is the inhalation of oxygen administered through the proper apparatus.

The treatment of those poisoned by vesicant gas is purely symptomatic, and the main object has been to impress upon medical officers the necessity of not overtreating these cases. It has been the aim of this office to disseminate a knowledge of the simple essentials of the treatment of the gassed.

5. The question of the hospitalization of the gassed was a more complicated one. Like the wounded soldier, the gassed soldier needs early examination and treatment, and it soon became obvious that each division in active warfare must have a mobile gas hospital as a part of its sanitary train. This need was met by utilizing one field hospital per division which was supplied with the necessary extra equipment to care for the gassed. Much correspondence and conference with those in authority finally led to a simple and standard equipment which could be used in divisional gas hospitals. The matter of the secondary hospitalization of gassed cases was complicated by the promulgation of the principle that gassed cases were not to be cared for in evacuation hospitals (fourth indorsement to letter from senior consultant in general medicine to chief consultant, Medical Services, May 7, 1918), although it was recognized that the gassed need special care in a hospital at the level of the evacuation hospital, quite as do the wounded.

The application of this principle led to the establishment of special hospitals for the gassed. During the actions which preceded the St. Mihiel and Argonne-Meuse battles there were no special hospitals for the care of the gassed. Gassed cases were passed through the evacuation hospitals rapidly and often received their first hospital treatment at the bases, a system which was unsatisfactory at best. In the St. Mihiel action one gas hospital was established at the Justice hospital center at Toul and one in the French gas hospital at Rambluzin. The personnel of these hospitals was composed of casuals or of officers and men loaned from base or evacuation hospitals, ambulance companies, etc. In each hospital one officer thoroughly conversant with the principles of the care of the gassed was stationed. At Toul, Lieut. R. M. Wilder, M. C., was in charge of the care of the gassed, and at Rambluzin Lieut. D. P. Barr, M. C., was director. The consultant in general medicine for gas poisoning had general supervision of the clinical work in both hospitals.

6. During the battle of the Argonne, five hospitals were designated by the chief surgeon to receive gassed cases. These were:

	Capacity beds
Rambluzin.....	250
La Morlette.....	550
Julvecourt.....	400
Rarecourt.....	250
Villers-Daucourt.....	200

The officers and personnel of these hospitals as in the previous action, were largely casual officers and men from ambulance companies, evacuation hospitals, etc. Early in September, 1918, the consultant in general medicine for gas poisoning was appointed director of gas hospitals in the First Army by verbal order of Lieut Col. L. C. Garcia, M. C., representative of the chief surgeon, First Army. He acted in this capacity until the cessation of hostilities on November 11, 1918. Lieut. D. P. Barr, M. C., was made commanding officer and clinical director of the hospital at Julvecourt, and Lieut. R. M. Wilder, M. C., held the same position at Rarecourt. These hospitals were both enlarged by the addition of tentage and became the most important gas hospitals in the area.

It is proper here to point out the very high character of the services rendered by these two officers. Their commands were new to the gas problem and inadequate in numbers, yet they developed their hospitals to a very high degree of efficiency, exhibited talent for leadership and administration, in the meantime directing the clinical work of the hospitals. Their enthusiasm lent a fine spirit to their respective organizations, and under their command these two hospitals attained a high state of efficiency.

After the first rush was over these five gas hospitals carried on the care and treatment of the gassed in an eminently satisfactory manner. It was unfortunate that, owing to a shortage of nurses, only two nurses were available for use in these gas hospitals during the period from September 26 to November 11.

7. These hospitals received upward of 20,000 patients from the 26th of September, 1918, to the 11th of November, 1918. The cases were about equally divided between those who had been actually exposed to gas and those who, though they entered the hospital with a diagnosis of "gassed," had in all probability never been exposed to toxic warfare gases. The bulk of gas cases were due to mustard gas (dichlorethylsulphide), a small proportion were due to suffocative gases (phosgene or chloropierin) and many were due to the inhalation of mixed gases (sneezing or tear gas, with or without one of the lethal gases). The large number of cases who could not be classified as "gassed" were due principally to exhaustion neuroses, light respiratory infections, or other unimportant conditions. The great proportion of these men could have been returned to duty without having left the army area had the proper machinery for this existed. In order that these light cases shall be returned to duty, rest camps must exist. Only one of the three corps in the First Army established a rest camp where men presumably fit for duty could be returned from the gas hospital and be further observed and tested before returning to the replacement battalion and the line.

One corps had a replacement battalion and no rest camp, while the third had neither replacement battalion nor rest camp. With this imperfect machinery it is natural that large numbers of men who could have been returned to duty perforce were evacuated to the bases.

8. The effect of the treatment received in the army gas hospitals during this period on the condition of the men sent to the bases was apparent. There were found in the bases less

serious eye conditions than ever before, burns of the skin were in better condition, and cases of lung involvement were received in better general condition. Each case of definite pulmonary irritation was considered as a possible pneumonia and was held at the gas hospital for observation and treatment until it was deemed safe for the case to be evacuated.

The lessons learned during this period lead to the following conclusions:

(a) At least 1,000 beds for gas cases should be provided for each corps during active mobile warfare such as that of September and October of this year.

(b) To facilitate evacuation and to economize personnel, not more than one hospital to a corps area is considered advisable. Experience has shown that the principle of having gassed cases cared for in special isolated hospitals is not a wise one. These hospitals were usually far from a railhead, and off the main traffic routes. This necessitated much extra ambulance carriage, and increased the length of time that patients were in the ambulances. As no provision for gas hospitals was found in the Tables of Organization, these scattered units had to be operated as annexes to evacuation hospitals. This arrangement complicated the administration of these hospitals, and required duplication of administrative personnel. Experience has shown that the recommendation to the effect that gassed be cared for in evacuation hospitals with augmented equipment and personnel, made in the letter of May 7, 1918, from the senior consultant in general medicine to the chief consultant, Medical Services, was sound, and should be accepted as a guiding principle in the matter.

(c) The personnel of gas hospitals should be proportionately the same as that of an evacuation hospital. The staff of medical officers need not be large; no surgeons are necessary. A chief of Medical Service expert in the problems of the diagnosis and treatment of the gassed and in the sorting of those presumably fit for duty is essential. The rest of the officers may be young men of ordinary capacity. Nurses are absolutely necessary for the proper care of the gassed.

(d) In order that men may be returned to duty, rest camps where the men may be observed for a time and tested by simple exercises to determine their fitness for duty are necessary. Whether the rest camp shall be under the immediate management of the corps or of the army is still open to discussion. Attention is invited, however, to the fact that while divisions change rapidly and frequently from one corps to another, they do not as frequently or as rapidly leave an army area. For this reason it would appear that the army would be able to return the men to their proper organizations better than could the corps.

10. In June, 1918, after conference between the medical director of the Chemical Warfare Service, American Expeditionary Forces, the chief consultant, Medical Services, American Expeditionary Forces, and the consultant in general medicine for gas poisoning, it was recommended that each division have one officer whose especial duty was to take charge of the organization of the treatment, care, and evacuation of the gassed within the divisional areas. The officer was to be known as the divisional medical gas officer. This recommendation was accepted and authorized by General Order No. 144, paragraph 8, subparagraph (b), August 29, 1918. Owing to the late date at which the divisional medical gas officers were authorized, many divisions never received the full benefit of the services of such an officer. In those divisions where an officer functioned as medical gas officer the care of the gassed immeasurably improved.

It is impossible to leave this subject without mention of Capt. Jasper Coghlan, M. C., who, under the authority of Col. J. W. Grissinger, M. C., functioned as medical divisional gas officer to the 42d Division and later as medical gas officer to the First Corps. Owing to the wisdom, foresight, and energy of this officer, the care of the gassed has been, first in the 42d Division and later in the organizations passing through the First Corps, the best in all the American Expeditionary Forces. It is the opinion of the writer that Captain Coghlan performed a most distinguished service and exerted a most important effect in the development of the early treatment of the gassed in the divisions throughout the American Expeditionary Forces.

11. Little is known of the late results of gassing. We do not know whether any of these men will become permanent invalids or not. It was hoped that opportunity would be found to study these cases in France, so that this question, which will be an important one to the Nation, might be definitely decided. The changes incident upon the cessation of hostilities defeated this aim.

It is therefore recommended that a sufficiently large group of soldiers who are in Class B, C, or D as a result of gassing should be sent to United States General Hospital No. 9, at Lakewood, N. J., for study and treatment. This office is ready to undertake the selection of these cases, and to supply the personnel necessary for the work. The transfer can be arranged by the system of tagging now in operation at United States Base Hospital No. 8, Savenay.

RICHARD DEXTER,
Lieutenant Colonel, M. C.

REPORT OF MEDICAL GAS WARFARE BOARD

AMERICAN EXPEDITIONARY FORCES,
HEADQUARTERS SERVICES OF SUPPLY,
OFFICE OF CHIEF SURGEON,
October 31, 1918.

Memorandum for Col. H. I. GILCHRIST,
President, Medical Gas Chemical Warfare Board.

In connection with Special Orders 291, paragraph 128, the chief surgeon desires that the following subjects be carefully considered and that recommendations be made covering the same:

1. Methods to segregate gas cases from malingerers or suspected gas cases.
2. Standardize the equipment for treating gas cases in the following:
 - (a) Camp infirmaries (par. 867, M. M. D.).
 - Regimental hospitals (par. 872, M. M. D.).
 - Ambulance companies (par. 874, M. M. D.).
 - Field hospitals (par. 879, M. M. D.).
 - Camp hospitals (par. 886, M. M. D.).
 - Evacuation hospitals (par. 891, M. M. D.).
 - Base hospitals.
 - Hospital trains.
 - (b) In considering these different units, recommendation will be made for such additional equipment to treat gas casualties, in all cases the equipment to be assembled as separate and distinct so that it can be removed at any time.
3. Consider the equipment for medical officers in treating gas cases in the advanced areas at the base.
4. Consider the equipment for the enlisted men of the Medical Department on duty with advanced units at the base.
5. Consider the subject of publishing orders dealing with the handling of gas cases from the time they are subjected to the fumes of poisonous gases until finally disposed of.
6. Consider the subject of awarding wound chevrons for men gassed; if entitled to chevrons for being gassed, should a time element be considered.
7. Consider the subject of training the troops in first aid to the gassed, etc.

WALTER D. McCaw,
Colonel, M. C., United States Army,
Chief Surgeon, American Expeditionary Forces.

AMERICAN EXPEDITIONARY FORCES,
HEADQUARTERS, FIRST ARMY,
November 5, 1918.

From: The medical gas warfare board, American Expeditionary Forces.

To: The chief surgeon, American Expeditionary Forces.

Subject: Report of meeting.

1. In compliance with Special Orders 291, paragraph 128, General Headquarters, American Expeditionary Forces, October 18, 1918, copy herewith inclosed, the medical gas warfare board of the American Expeditionary Forces convened at headquarters, First Army, November 5, 1918, all members of the board being present.

2. Letter of instructions from the chief surgeon of the American Expeditionary Forces to the president of the board and subjects to be considered were taken up and action taken as follows:

Paragraph 1. All gas cases received at divisional gas hospitals should be examined by the personnel of the hospital; all doubtful cases should be referred to the division medical gas officer, who shall consult with the division psychiatrist where there is any question of gas, shock, or exhaustion. After a maximum period of 24 hours those cases showing no symptoms of contamination with gas shall be returned to duty. All cases showing signs of the toxic effects of gas shall be evacuated to army gas hospitals, where a redistribution shall be made in the shortest possible time to either base hospitals, battalion replacement stations, or corps rest hospitals. This procedure is deemed necessary in view of the fact that approximately 80 per cent of the cases received at the field gas hospitals are suffering from causes other than gas; i. e., shock and exhaustion, influenza, etc.

Paragraph 2. One field hospital in each division shall be designated as a gas hospital. Additional to equipment C for field hospitals, Medical Department Manual, 1917, paragraph 897, certain extra equipment will be supplied to these hospitals. One additional truck must be provided to carry this additional equipment. Appended is a list of extra equipment needed for the care of gassed in the different stations and hospitals in divisional and army areas.

Paragraph 3. In the advanced area medical officers shall carry, in addition to regulation equipment, 1 box of ammonia ampules; medical officers at base need no extra equipment.

Paragraph 4. It is recommended that noncommissioned officers in all organizations in forward areas be required to carry 1 box of ammonia ampules for the first aid to suffocative gas cases. Instruction in the use of above will be given by division medical gas officers. No extra equipment required at base.

For enlisted men, in excess of the present equipment, 1 box of ammonia ampules is required; for all litter bearers, 1 M-2 French mask, in addition to the box respirator, is to be carried and to be applied to casualties who are unable to retain the mouthpiece of the box respirator.

Paragraph 5. Space in present report too limited for detailed requirements of paragraph 5. It is suggested that special circular to division medical gas officers be issued through the medical director, Chemical Warfare Service, to the chief surgeon, American Expeditionary Forces.

Paragraph 6. Covered by separate report.

Paragraph 7. No remarks.

MEDICAL GAS WARFARE BOARD,

H. L. GILCHRIST,

Colonel, M. C., United States Army,

H. H. M. LYLE,

Lieutenant Colonel, M. C., United States Army,

RICHARD DEXTER,

Major, M. C., United States Army,

JASPER COGHLAN,

Captain, M. C., United States Army.

List of extra equipment needed for the care of gassed in the different stations and hospitals in divisional and army areas ^a

	Regimental aid station, Infantry and Artillery	Battalion aid station, Infantry	Advance aid post, Infantry	Battalion aid post, Artillery	Battery position	Ambulance	Field gas hospital	Evacuation hospital
Albolene.....pounds.....							1	2
Alcohol (solid).....cans.....	5	5					12	
Ammonia ampules.....boxes.....	10	5	5	5	5	10	100	
Aprons, rubber.....							2	
Atomizers (oil).....							2	6
Bags, personal belongings.....							500	1,000
Bed sacks.....							200	
Boots, rubber hip.....							4	4
Cans, irrigating, enamel.....							2	6
Caffeine, sodium benzoate.....ampules.....	25	25	25	25	25		50	100
Camphor in oil (14-16 F).....do.....	10	10	10	10	10		50	100
Catheters, soft rubber.....	4	4	2	4	4	4	20	20
Clippers, hair.....							6	6
Coats, antigas.....	6	6	6	6	4	2	6	6
Digitaline Nativele (25 mgm.).....							50	100
Droppers, medicine.....							1	2
Fans, antigas.....	2	2	2	2	2			
Gloves, rubber, post-mortem.....pairs.....							6	6
Hats, antigas.....	6	6	6	6	4	2	6	
Lime chloride.....pounds.....	50	50	25	50	50		100	
Masks, French M-2.....	6	6	6	6	6	4	100	
Menthol (1 ounce).....							2	2
Mittens, antigas.....pairs.....	6	6	6	6	4	2	10	10
Novocaine 2 per cent.....ounces.....							2	2
Nozzles, irrigating.....							12	12
Overalls, antigas.....	6	6	6	6	4	2	6	6
Oxygen breathing apparatus, American.....	1		1	1	1		2	2
Oxygen breathing apparatus, Haldane 2-way.....							2	4
Oxygen tanks, 1,500 liters.....							6	12
Oxygen tanks with hose connection, 500 liters.....	1	1		1	1		6	6
Pajama coats.....								250
Pajama trousers.....								250
Pinch cocks.....							10	20
Respirators, box.....	(^b)	(^b)	(^b)	(^b)	(^b)		(^b)	
Respirators, Tissot.....	3	3	2	2	2			
Shower heads and piping.....							4	8
Shovels.....	1	1	1	1	1		2	
Soap, alkaline, bath.....pounds.....							50	100
Sodium bicarbonate.....do.....	2	2	2	2	2		20	30
Sodium chloride.....do.....	2	2	2	2	2		15	25
Sponges, bath, sea.....							6	12
Sterilizer, Foden-Thresh or American.....								1
Stoves, Primus.....							4	6
Sphygmomanometer.....							1	1
Signal, gas, Klaxon.....	1	1	1	1	1		1	
Tags, paper, "gas clothing".....							500	
Talcum powder.....pounds.....							25	50
Towels, bath.....							500	500
Tubing rubber 3/8 inch inside.....feet.....	4	4	4	4	4		15	20
Tubing, hose, 1 inch inside.....do.....							6	6
Tubing, glass, 4-inch sections, 1/4 inch inside.....	4	4	4	4	4		50	
Twines, balls.....							2	
Veronal tablets.....							100	200
Water heater, French.....							1	2

^a For other supply lists see pp. 76, 77, 832.—Ed.

^b 5 per cent extra of number of personnel.

APPENDIX NO. 8^c

AMERICAN EXPEDITIONARY FORCES,
HEADQUARTERS FIRST ARMY,
France, November 5, 1918.

From: The medical gas warfare board, American Expeditionary Forces.

To: The chief surgeon, American Expeditionary Forces.

Subject: Wound chevrons for gassed cases.

1. In compliance with Special Orders, 291, paragraph 128, General Headquarters, American Expeditionary Forces, October 18, 1918, the medical gas warfare board convened on November 5, 1918, for the purpose of considering the question of the awarding of wound chevrons to men who have been gassed.

2. After carefully considering the subject, it is the opinion of the board that those who have become actually incapacitated from the effects of enemy warfare gases through no fault of their own should be given the same recognition as those who have been wounded. It is, however, the opinion of the board that certain restrictions must be made in awarding wound chevrons to gas casualties, for the reason that under the present system of award many men who have never been incapacitated by enemy gas are wearing the distinctive mark of those wounded on the field of battle.

3. In order that wound chevrons may be justly awarded, it is recommended that no soldier be given a wound chevron who has not been treated in an army hospital for a period of at least 10 days, and then only on the recommendation of the commanding officer of such hospital or hospitals.

4. It is further recommended that this principle be retroactive for the period during which the American Expeditionary Forces have been on active duty in the present conflict.

MEDICAL GAS WARFARE BOARD,

H. L. GILCHRIST,

Colonel, M. C., United States Army.

H. H. M. LYLE,

Lieutenant Colonel, M. C., United States Army.

RICHARD DEXTER,

Major, M. C., United States Army.

JASPER COUGHLAN,

Captain, M. C., United States Army.

LIST OF ARTICLES REQUIRED BY DIVISIONS FOR THE TREATMENT OF GAS CASES^e

GENERAL HEADQUARTERS,
AMERICAN EXPEDITIONARY FORCES,

France, June 27, 1918.

Memorandum to those concerned from representative of the chief surgeon with G-4, G. H. Q.

These articles should always be immediately available, and preferably turned over in bulk to one of the field hospitals of each division which under present conditions is specially designated for the treatment of this class of cases. It should be pointed out that we can not wait until gas cases begin to flow in before ordering up this necessary equipment. It should be furnished at once and kept at the front in the hospitals mentioned.

Ambrine.....	1/2-pound cakes..	100	Sheeting, rubber.....	yards..	20
Digitalinum, hypo-tabs.....	tubes.....	50	Syringes, fountain, metal.....	number..	6
Petrolatum.....	3-pound tins..	50	Tubs, bath, portable.....	do..	2
Sapo Mollis.....	1-pound bottles..	200	Transfusion sets (furnished by central		
Petrolatum, liquid.....	do.....	40	Medical Department laboratory, 721)		
Sodium carbonate.....	pounds.....	440	number..	3
Brushes, paint (furnished by Medical			Clothing, complete sets.....	sets..	1,000
Department).....	number..	2	Stoves, small.....	number..	3
Litters.....	do.....	200	Gas masks (furnished by G. M. C. and		
Medicine droppers.....	do.....	48	other departments. Gas masks to be		
Oxygen, 5,000-liter tanks.....	do.....	5	turned over to division gas officer)		
Oxygen inhalators.....	do.....	6	number..	2,000
Oxygen cylinders, small.....	do.....	6	Baths, shower, portable.....	do.....	2

A. D. TUTTLE, *Lieutenant Colonel, Medical Corps.*

^c This part of the report of the medical gas warfare board appears as an appendix, p. 170, Vol. II, History of Chemical Warfare Service, American Expeditionary Forces.—Ed.

^e For other supply lists see pp. 76, 77, 831.—Ed.

CIRCULAR NO. 34, AMERICAN EXPEDITIONARY FORCES (RÉSUMÉ OF SYMPTOMS AND TREATMENT OF POISONING BY IRRITANT GASES) ^a

AMERICAN EXPEDITIONARY FORCES,
OFFICE OF THE CHIEF SURGEON,
France, June 12, 1918.

The following information will be given the widest possible circulation among the medical officers of the American Expeditionary Forces. Each medical officer should possess and keep at hand a copy of this circular: "Short résumé of the symptoms and treatment of poisoning by irritant gases."

The gases which have been met with most commonly up to the present time may be divided schematically into three classes:

- (1) Suffocative gases, which exercise their main effect on the lung tissue (chlorine, phosgene, diphosgene, chloropierin).
- (2) Vesicants, the prime effect of which is exercised upon the skin conjunctivæ and upper air passages (dichlorethylsulphide, mustard gas or yperite).
- (3) Pure lacrymatory gases (xylyl-bromide).

Gas may be liberated from cylinders in clouds, a method not now commonly employed, or from shells.

"The general aim of the enemy in the present use of gas shells is to fire simultaneously shells of different types, some of which will cause so much sensory irritation that the man will discard his respirator and then become vulnerable to lethal shells, phosgene, and similar substances. Owing to this mixture of shells the symptoms reported by patients are often very confusing."

NOTE.—Much of this material has been extracted from the valuable reports of the British chemical warfare medical committee and from the excellent report of Lieut. Col. H. L. Gilchrist, issued by the office of the chief of the gas service, American Expeditionary Forces, March 15, 1918.

For this purpose several arsenical compounds have been tried.

SYMPTOMS OF GAS POISONING

SUFFOCATIVE GASES

Suffocative gases, which are relatively nonirritative on inhalation in the concentrations ordinarily used, induce some hours after their entrance an intense edema of the lungs. Through the great outpouring of fluid into the lung tissue the patient drowns in his own serum; the blood becomes greatly condensed and viscous; there is marked polycythemia; the capillary flow is obstructed; thromboses are not uncommon, a greatly increased strain is put upon the right heart; the patient suffers from intense oxygen want.

SEQUENCE OF EVENTS

"The immediate effects of irritation of the eyes may be prominent at first, but as a rule quickly pass off; within 3 to 12 hours after exposure to the gas the main symptoms, asphyxia and prostration, due to affection of the lung alveoli and accumulation of fluid in them, appear. In this state the patient's respiration is rapid and usually accompanied by pain (often intense) in the chest; there may be fits of coughing, but the amount of expectoration is very variable, being profuse in some cases and very scanty in others; in the more severe cases the patient is restless and anxious, or may be semicomatose, with muttering delirium. Therefore many patients will be unable to give a definite account of their symptoms, as loss of memory of immediate events may last for several days. Patients with severe pulmonary edema fall into two groups.

^a Copy on file, Historical Division, S. G. O.

"(a) Those with definite venous engorgement. In these the face is congested, the lips blue, and the superficial veins of the face may be visibly distended. There is true hyperpnea; i. e., the breathing is not increased in frequency but the actual amount of air reaching the lungs is greater than normal. The pulse is full and of good tension, and the rate is not often much above 100.

"(b) Those with collapse. In these the face is pale and the lips of a leaden color. The breathing is shallow, so that there is but little true hyperpnea. The pulse is rapid (130 to 140) and weak.

"In patients who recover, the edema fluid is absorbed within a few days; in some cases signs of bronchitis or bronchopneumonia, due to a secondary infection, persist for some time, but in most cases the lung returns to a condition which is normal except for the presence of some disruptive emphysema. In consequence, however, of the edema of the lungs during the early stage, deficient oxygenation of the blood occurs, unless prevented by the administration of oxygen. The deficient oxygenation gives rise to widespread temporary injury in the various systems.

"2. *Vesicants*.—The only one hitherto employed is dichlorethylsulphide, an oily liquid used in shells, and scattered from them on the ground, where it slowly evaporates. This not only attacks those in the immediate vicinity of the shell burst, but may affect those who may walk over the contaminated ground later. The fluid may be spattered also on clothing, shell casings, rifles, etc., and may thus become effective through direct contamination of the skin.

"The main action of this group is an irritant one on the skin, eyes, and respiratory passages.

"*Special symptoms*.—(a) *Early*.—These are insignificant, nothing being noticed immediately except a smell reminiscent of mustard, from which the gas derives its name (mustard gas). A soldier may not realize for many hours that he has been exposed to gas, until the more important delayed symptoms develop.

"(b) *Delayed*.—These are the principal symptoms of this group and appear 3 to 24 hours after being gassed. They occur usually in the following order, and approximately after the intervals stated.

"(i) *Conjunctivitis* (3 hours). This rapidly becomes very acute, and is accompanied by intense photophobia, and swelling of the lids, which may cause closure of the eyes for days.

"(ii) *Vomiting and epigastric pain* (4 to 8 hours). These symptoms appear together, as a rule, and are apt to be persistent and intractable.

"(iii) *Burns* (12 hours). Widespread erythema with local vesication occurs, going on to definite burns. The commonest sites are the axillæ, genitals, and back, but no area may be exempt. The affected surfaces frequently develop very marked pigmentation. Deep burns sometimes occur when the liquid itself comes into contact with the clothes or skin.

"(iv) *Laryngitis, pharyngitis, tracheitis, and bronchitis* (24 to 48 hours). These are the most dangerous symptoms. The degree and extent of the lesion may vary from a simple irritation of the surface to an ulceration of the mucous membrane of the whole passages, followed by infection of the raw surfaces. These conditions may be so extensive and severe as to cause death by themselves or in consequence of the development of bronchopneumonia.

"In a certain number of cases with severe involvement of the respiratory organs, which recover, there has evidently been some interference with the proper oxygenation of the blood, which may give rise eventually to symptoms resembling the after effects of the suffocative gases. * * *

"When a soldier is protected by the respirator, the respiratory and eye symptoms are absent or slight."

TREATMENT

SUFFOCATIVE GASES

The grave symptoms here are due mainly to the intense pulmonary edema. The conditions which we have to combat are essentially: (a) Oxygen want; (b) condensation of blood; (c) overburdening of the right heart.

Our main aims are: (a) Rest; (b) warmth; (c) oxygen; (d) bleeding;

(a) *Rest*.—Protect the patient from all unnecessary physical effort in order to reduce the oxygen need. Do not disturb him at the advanced aid station by questioning; his life may depend on the care with which he is handled in the early stage.

All the gassed should be stretcher cases.—Small oxygen tubes, if available, should be carried in each ambulance in the proportion of one to each stretcher case, and exchanged at the evacuation hospital for freshly filled tubes; these can of course be used only when the ambulance has passed out of the gassed area.

Give the patient fresh air. Do not close the ambulance too tightly unless it be very dusty.

(b) *Warmth.*—Warmth is important. Cold and shivering mean an increased production of CO₂ and an increased demand for oxygen. The clothes must be removed at the earliest moment, *for they hold gas and may be dangerous not only to the patient but to those about him*; warm covering must, however, be provided.

(c) *Oxygen.*—The administration of oxygen in all dyspneic, cyanotic patients is of vital importance. The administration should be so nearly continuous as possible up to the point of the disappearance of the cyanosis, and should be continually repeated whenever the demand is evident.

(d) *Bleeding.*—In patients who are cyanotic and show engorgement of the venous system, bleeding is indicated. By venesection we combat—

(1) Edema of the lungs.

(2) The condensation of the blood; for with the abstraction of the polycythemic blood, fluid is drawn from the lungs and the tissues, and the circulatory medium becomes less viscous.

(3) The overburdening of the right heart.

The bleeding should be early and free from 2 to 600 c. c.

Bleeding is inadvisable, nay dangerous, in the patient who is pale and gray and in collapse.

If the heart's action be rapid or feeble, bleeding may be preceded by an intramuscular injection, 15 minutes before the venesection, of one-fourth milligram ($\frac{1}{2}\frac{1}{10}$ grain) Digitaline cristallisee Nativelle. This may, if necessary, be repeated once or twice in the next 24 hours, and continued later by the mouth if necessary.

In the early stages, during the period of distressing restlessness and agitation and pulmonary edema, morphia may be necessary. Its action as a respiratory depressant is believed by some to be dangerous; and the administration of oxygen, if it suffices, is the safest and best means of quieting the agitation. Where the distress and physical effort associated with the struggles of the patient are great, morphia 0.016 ($\frac{1}{4}$ grain), hypodermically, may be demanded, but at the same time it should be remembered that in collapse, dulling of the respiratory center may turn the scale against the patient.

TREATMENT OF THE PALE, GRAY CASES, WITH COLLAPSE

Oxygen is here the main aim, and the administration should be practically continuous. *Never bleed these patients. Bleed only those with venous congestion.*

Rest, warmth, and oxygen are the mainstays of treatment. Atropine and adrenaline are contraindicated. These drugs place an increased strain on the heart. It is best to abstain from intravenous salt solution injections. The fluid introduced puts an extra burden on the heart, is soon absorbed into the tissues, and may increase the pulmonary edema. In grave cardiac weakness, preparations of camphor or caffeine may be given hypodermically, and digitalis may be indicated, according to the nature of the case.

RELAPSES

In any patient who has had pulmonary edema it may, within the first few days, recur on slight exertion or even without apparent cause, and if there have been any definite symptoms of edema of the lungs the patient should be kept in bed for a week.

Smoking should be absolutely prohibited, and convalescents should not be allowed to smoke in the ward in which these patients lie.

Patients whose symptoms have been mild should, if possible, be put on graduated exercises as soon as they are out of bed, and under military discipline as soon as possible. Mild cases should be back in the line in about two weeks. Severe cases may have to remain in the hospital for three or four weeks and thereafter spend several weeks in a convalescent camp.

Great care should be taken to protect the convalescent from secondary infections. Wherever it is possible beds should be isolated one from another by sheets, as in acute respiratory infections, for secondary bronchitis and bronchopneumonia are not uncommon and the danger of cross infection should be provided against.

VESICANT GASES

The symptoms, here, are usually delayed from 3 to 24 hours, and dangerous symptoms do not, as a rule, appear for from 24 to 48 hours after exposure, but pulmonary edema and symptoms similar to those observed in the suffocative cases may occur; moreover, the patient may have had a double exposure to different sorts of gas. All the precautions, therefore, above mentioned should be observed at the outset, but other special steps must be taken.

DISPOSITION OF CLOTHES

Wherever exposure to a vesicant gas is suspected, the use of external warmth should be avoided if the clothes have not previously been removed. The application of heat favors the diffusion of the gas.

Remove the clothes as soon as possible but protect the patient from exposure during the process.

After removal, the clothes should be sterilized in wet steam for 30 minutes; in dry heat for 15 minutes; exposed to the air for 15 minutes. This may be carried out in the Thresh sterilizer, and may have to be repeated twice, although two or even one treatment may be efficacious. While waiting for sterilization, have the clothes placed outside the quarters, in the open. All who handle the clothes must be protected by respirators and special oiled clothing and gloves.

REMOVAL OF THE POISON FROM THE SKIN

The patient should be thoroughly bathed in a warm room in soap and water at the earliest possible moment. Areas which have been specially exposed may first be covered for a few minutes by a paste of 25 to 50 per cent chloride of lime in water and then washed with warm water. Bathing with 0.05 per cent permanganate of potassium is said to be useful.

TREATMENT OF THE SKIN AND MUCOUS MEMBRANES

When the skin is dry, erythematous areas may be powdered with subnitrate or subcarbonate of bismuth, oxide of zinc, talcum, or any simple nonirritating powder. Moist and raw surfaces may also be powdered with the same substances, or a powder consisting of oxide of zinc, carbonate of magnesia, carbonate of lime, 200 grams; talcum powder, 400 grams, and protected from the bedclothes by cribs, or covered by a nonabsorbent dressing.

If a moist dressing be preferred a solution consisting of sodium chloride, 70 grams; sodium bicarbonate, 150 grams; water, 5,000 grams, may be used—simply limewater.

Blisters should be carefully attended to. *The contents of the vesicles are poisonous and irritating to the surrounding skin;* the blisters should, therefore, be opened carefully and the contents taken up with absorbent cotton, which should promptly be burned. Interdigital areas should be washed carefully daily, powdered, and bandaged.

Fatty salves, in the early stages, are inadvisable, as any underdestroyed poison which remains on the skin may be diffused underneath.

Later, deep and painful burns are much relieved by treatment with ambrine.

The eyes should be irrigated immediately with warm alkaline solutions such as the above-mentioned solution of sodium chloride, sodium bicarbonate, and water. After this some nonirritating oil such as liquid albolene should be instilled. The patient should be kept in a dark room or the eyes shaded. Compresses soaked in this solution may give comfort in the acute stage. In severe cases, frequent (every two to three hours) irrigation of the conjunctiva with simple boric solutions (sodii boratis, 65; aquae camphorae, 30) followed by the instillation of liquid albolene should be carried out.

The nose should be sprayed with a warm alkaline solution (sodium chloride, sodium bicarbonate and water, as above) and also with liquid albolene, to which a little menthol may be added (such as the preparation known as "ehloreton inhalant").

The mouth should be rinsed with alkaline washes and gargles.

The laryngeal inflammations may be relieved by inhalation of menthol, 0.65; tinct. benzoini comp. ad 30, of which 5 c. c. are added to 500 c. c. steaming water.

SECONDARY RESPIRATORY INFECTIONS

"Mustard" cases may develop grave secondary bronchitis, with bronchopneumonia. In the treatment of such instances there is nothing specific. Every precaution should, however, be taken to prevent cross infection. The beds of all patients with purulent bronchitis and bronchopneumonia should be screened one from another and from their neighbors.

SEQUELS OF GAS POISONING

In soldiers who have been "gassed," especially with phosgene, symptoms similar to those characterizing D. A. H. (effort syndrome) are not uncommon—dyspnea on exertion—pain in the chest, palpitation, dizziness, fatigue on exertion, disturbed sleep with dreams, paroxysms of coughing, and even asthmatic attacks. These patients are often polycythemic. Nervous manifestations unassociated with apparent organic lesion are common.

Get these patients out of bed and start carefully graduated exercises, sending them as soon as possible to a special training camp.

"Functional" photophobia and blepharospasm are frequent, but eye shades and colored glasses should be discontinued as soon as the acute inflammatory stage is over. When this has passed the use of eyedrops of a solution of:

Zinci sulphatis.....	0.065-0.13 (gr. I-II)
Acidi borici.....	3.75 (3T)
Aquæ.....	30 (3T)

is said to give relief. If corneal ulcers or iritis which are not common be present, they must be treated in the usual manner. Threatening though the ocular manifestations may be, recovery is usually complete. Grave damage to the uveal tract is rare. It is important not to overtreat the eyes.

In all cases preserve an optimistic attitude; the great majority of gassed patients recover completely.

Do not let the patients become introspective or "hospitalized." Keep them occupied in mind and body. Get the "mustard" gas cases who have no respiratory involvement out of bed in two or three days if possible. Remove the eye shades as soon as the acute inflammatory stage is over. Send the men out of doors, look out for their employment or amusement, and get them under army discipline as soon as may be. Far too many convalescent "gassed" cases tend to accumulate, uncared for, in base hospitals. The responsibility of the medical officer does not end with the disappearance of the dangerous symptoms. See to it that the patient does not become a psychoneurotic.

Attention to these details may save a considerable wastage of men.

M. W. IRELAND,
Brigadier General, Chief Surgeon.

**REPORT OF LECTURES FOR DIVISION MEDICAL GAS OFFICERS HELD IN PARIS
IN OCTOBER, 1918^a**

AMERICAN EXPEDITIONARY FORCES,
HEADQUARTERS SERVICES OF SUPPLY,
OFFICE MEDICAL DIRECTOR, CHEMICAL WARFARE SERVICE,
October 15, 1918.

From: Medical director, Chemical Warfare Service.

To: Chief surgeon, American Expeditionary Forces (through chief, Chemical Warfare Service).

Subject: Report on special course of lectures for division medical gas officers.

I wish to make the following report concerning the special course of lectures for division medical gas officers which was given in Paris, October 7, 8, 9, and 10. This course was held at the amphitheater of the school of pharmacy, University of Paris. The daily session began at 9 a. m. and terminated at 5 p. m., with two hours intermission at midday. In addition to the prospective division medical gas officers ordered to attend, there were a great many others who took advantage of the course, thereby increasing the attendance to about 70 at each session. The course was conducted like a regular school course, roll call being held at 9 a. m. and 2 p. m. each day and all absentees being called upon to explain their absence.

The session was opened by Professor Rogers of the medical faculty of the University of Paris, who spoke very pleasingly to the class and took the occasion of extending to them and to the medical officers of the American Expeditionary Forces all the privileges of the laboratories, libraries, and other facilities of the university.

Lieutenant General Burtchaell, surgeon general of the British armies in France, was the next speaker. General Burtchaell spoke for about 15 minutes, during which time he took occasion to congratulate the Medical Corps of the American Expeditionary Forces on securing division medical gas officers. He emphasized the necessity for having such officers with divisions and spoke of their numerous duties and of the wonderful opportunities presented to them for early study of gas cases at the front.

Brigadier General Thayer, chief consultant, medical services, American Expeditionary Forces, then spoke to the class. He emphasized the necessity for division medical gas officers and the importance of their duties.

After the introductory part of the session, Major Zanetti, of the Chemical Warfare Service, lectured on "The relation of chemistry to medicine and the importance of the medical officer being familiar with gas chemistry." During the course of his lecture he exhibited specimens of the different chemicals and gases in use.

Major Flandin, of the French Medical Corps, was the next lecturer. His subject was "The operations of warfare gases, their effects, actions on animals, etc." His lecture was illustrated with moving pictures.

At 2 p. m. the class assembled at the University of Paris, where Aide-Major Mayer, of the Medical Department of the French armies, delivered two excellent lectures, his subjects being "The physiology and pathology of gassed patients." His lectures were illustrated by lantern slides and were extremely interesting.

He was followed by Major McCullough, of the Chemical warfare Service, American Expeditionary Forces, who lectured on methods by which gases were introduced and the importance of medical officers being familiar with them.

TUESDAY—SECOND DAY

The forenoon was devoted to the subject of "Lung irritants," and especially phosgene. Major Flandin, of the French armies, lectured to the class from 9 a. m. to 10 a. m. He was followed by Colonel Douglas, of the British armies, who lectured on the same subject, laying special stress on the action of oxygen in connection with the treatment of lung irritants. Colonel Norris, of the American Expeditionary Forces, lectured on the early symptoms and treatment of gas cases, emphasizing especially the necessity for and importance of early diagnosis and absolute rest.

^a Appendix 5, History of Chemical Warfare Services, American Expeditionary Forces, Vol. II, 162. Copy on file, Historical Division, Army War College.

The afternoon session was devoted to the subject of "Vesicants," especially mustard gas, the symptoms, and treatment. Major Clarque, of the French armies, was the first lecturer. He was followed by Colonel Pasteur, of the British armies, who not only lectured on this subject, but also dealt briefly with arsine poisoning, symptoms, and treatment. Colonel Lee, of the American Expeditionary Forces, followed Colonel Pasteur, and lectured on the late effects of mustard-gas poisoning, including vesicant actions and treatment.

Lieutenant Goldschmidt, of the Chemical Warfare Service, American Expeditionary Forces, spoke a few words on the results of animal laboratory experimentation with saline isotonic transfusion following blood letting. A general discussion followed his talk.

WEDNESDAY—THIRD DAY

The forenoon was devoted to organization and methods for the evacuation of gassed cases. Colonel Ashford, of the American Expeditionary Forces, was the first lecturer, his subject being "Evacuation hospitals and the facilities therein for treating gassed cases." Colonel Ashford was followed by Major Flandin, of the French armies, who spoke on the French methods of handling gassed cases. Colonel Douglas, of the British armies, next addressed the class on the British organization and methods for handling gassed casualties. He also spoke of the German organization for handling these cases. Following Colonel Douglas, Captain Coughlan, of the American Expeditionary Forces, spoke on the organization and duties of division medical gas officers as worked out in the 42d Division.

At 2 p. m. Captain Coughlan concluded his talk on this subject. At 3 p. m. Professor Achard, chief of the medical gas service of the French armies, spoke on the subject of "The late symptoms and treatment of mustard-gas poisoning."

The theoretical part of the session was closed by a few remarks by Col. H. L. Gilchrist, medical director of Chemical Warfare Service of the American Expeditionary Forces, following which a practical demonstration was given of the degassing unit, which took place in front of the School of Pharmacy.

THURSDAY—FOURTH DAY

Thursday was devoted to visiting different hospitals in Paris and studying the latest methods for the treatment of gassed cases.

In view of the marked enthusiasm displayed by the officers attending the course, it is believed that these courses should be conducted frequently. To that end it is recommended that a special medical gas course of lectures be added to the curriculum of the sanitary school at Langres, as this will give the medical officers of our services an opportunity to keep posted on this important subject. At the recent meeting all the latest medical methods in connection with warfare gases were introduced, especially those in regard to the treating of masses, their evacuation, etc.

In conclusion, I wish to take this opportunity of thanking the directors of l'Ecole de Pharmacie for the use of their buildings during this course; Dean Rogers, Professor Achard, Major Flandin, Captain Clarque, and Aide-Major Mayer of the French armies; Lieutenant General Burtchaell and Colonels Pasteur and Douglas, of the British armies; and Colonels Lee and Norris, Majors Zanetti and McCullough, and Captain Coughlan, of the American Expeditionary Forces, for their able assistance and help in connection with this first special gas course for our medical officers.

H. L. GILCHRIST,
Colonel, M. C., United States Army.

REPORT ON GAS HOSPITAL, JUSTICE HOSPITAL GROUP^a

[By Lieut. Col. Harry W. Goodhall, M. C.]

The gas hospital, Justice hospital group, was a provisional hospital and not an organized unit. Its formation was hastily planned in anticipation of the activities in the St. Mihiel sector to meet the requirements of an emergency. The hospital performed an active and useful service from August 29, 1918, to October 8, 1918, when it was taken over by Base Hospital No. 87.

On August 29, 1918, Lieut. Col. Harry W. Goodhall, M. C., Base Hospital No. 51, was temporarily relieved from duty with that organization by verbal orders of Lieut. Col. H. C. Maddux, commanding officer of the group, to assume command of the gas hospital. This order was confirmed by paragraph 1, S. O. No. 11, J. H. G., August 31, 1918.

On August 30, 1918, First Lieut. George W. Papen, M. C., Base Hospital No. 51, was temporarily relieved from duty with that organization and reported for duty at the gas hospital, in compliance with verbal orders confirmed by paragraph 2, S. O. No. 11, J. H. G., dated September 31, 1918. He was assigned to duty as adjutant, detachment commander, and mess officer.

On August 30, 1918, First Lieut. Russell M. Wilder, M. C., Evacuation Hospital No. 2, in accordance with telegraphic orders, commanding general First Army, reported to the commanding officer of the group and was assigned to the gas hospital for duty. He was assigned as chief of the gas service and as supply officer.

These three officers were the only permanent officers assigned to the hospital during its existence, and all of the administrative work and the burden of the medical work was carried on by them.

On August 30, 1918, 50 enlisted men from the special training battalion stationed at St. Aignan, then on duty with Evacuation Hospital No. 3, stationed at Toul, reported at the gas hospital in compliance with S. O. No. 7, Hdqrs. J. H. G., dated August 29, 1918.

* * * * *

On August 31, 1918, the following civilian help was engaged:^b

* * * * *

All of these women had been employed by the French hospital which occupied these buildings prior to their being taken over by the American Army. They worked from 7 a. m. to 11.30 a. m. and from 1 p. m. to 5 p. m. They had one day per week off and they were paid 6 francs a day. This arrangement was the same as that under which they had been employed by the French.

To supply the lack of noncommissioned officers, the following Medical Department men were assigned to the hospital:^b

* * * * *

The buildings selected for the gas hospital were those known as the Lamarche Annex and adjoined Caserne Lamarche. These buildings were originally constructed for hospitalization and in times of peace had been used by the French as the hospital for the entire garrison stationed here. On this account they were perhaps better arranged than the buildings that were occupied by the other hospitals in the group.

BUILDINGS

There were four large ward buildings, constructed of stone and concrete, a small administration building, two kitchens, and a large Bessonneau tent.

These ward buildings were not entirely fireproof, inasmuch as the floors were constructed of wood.

They were divided into rooms that would accommodate about 15 patients without crowding, and these rooms were well ventilated and very light. The possibilities of isolation were very good. The corridors and stairways were spacious. The four buildings would accommodate comfortably 1,000 patients, but owing to the lack of storerooms and mess accommodations it was only possible to prepare for a normal capacity of 650 beds.

^a Copy on file, Historical Division, S. G. O.^b Names omitted.—Ed.

In certain respects the buildings were very poorly arranged for hospitalization. Running water was to be found in but one room in each building, and there were no rooms fitted up as service rooms. There was no arrangement whereby even a liquid diet could be prepared. There was no arrangement in the buildings for the disposal of waste matters.

The administration building was sufficient for the purpose and also served as quarters for the officers.

Both kitchens were equipped with French ranges, which were not suited to our methods of cooking. To add to this obstacle the grate in one range was broken, and it was not until September 15 that it was repaired. During the latter part of September an Army range was installed in one of the kitchens, which added much to the service rendered, but even this was not sufficient to meet the demands made upon this department. The distance between the kitchens and the wards was a distinct handicap to good service. Liquids transported in bulk could be kept hot, but special measures had to be adopted with other foods. There was no means of keeping food hot once it arrived at the wards or of heating food in the wards until early in October, 1918.

The large Bessonneau tent was in excellent condition and well located for the purpose for which it was used, namely, as a triage and reception ward.

There was one small laundry operated by hand that could do a limited amount of small work.

The latrines were of the usual French type of can latrine, and these were emptied by French civilian contractors.

The water supply was from two sources. A tank situated on the area received water from the wells located on the area of Caserne Fabvier, and pipes had been extended from a tank situated on the area of Caserne Lamarche, which received water from the Moselle River, passing through a filter.

The sewer system consisted of a series of pipe lines and drains which received, through catch basins, rain water and liquids from the kitchens, baths, and urinals.

French civilian contractors had been employed to carry away garbage, and there was a good incinerator in the rear of the area.

As has already been stated, this hospital was formed in anticipation of activities in the St. Mihiel sector, and as originally planned it was intended to give initial treatment to gas casualties. Later events showed that this was a miscalculation, which experience would have recognized immediately, inasmuch as Toul was about 15 miles from the nearest point to the front line. As a matter of record only 169 cases out of a total of 1,281 came to the hospital without first passing through a field hospital where the initial treatment was given. Furthermore, it was thought that the gas casualties would be the first to arrive in the group, and the commanding officer was instructed to have the hospital clean and with 650 beds set up and ready for patients within 72 hours.

Lieutenant Wilder was assigned to the hospital because he had had long and intensive experience in the handling of gas casualties at Baccarat, where Evacuation Hospital No. 2 was located. For this reason the plans as to the arrangement of the hospital and the selection of the equipment were left largely in his hands.

Within 48 hours the hospital was clean and the required number of beds set up and ready to receive patients. Within 11 days, the date the first patient was admitted, the hospital was fairly well equipped and the weak points of the hospital had been recognized.

The arrangement of the hospital was as follows:

The Bessonneau tent was used as the triage and as a receiving ward. In one corner of the tent a room was screened off for the treatment of cases of phosgene-gas intoxication. In this way the patient was spared unnecessary handling, oxygen could be administered promptly, and, if necessary, phlebotomy done at once. This room was promptly fitted up and all the necessary equipment obtained.

Building B was set aside for these cases as soon as their condition permitted their being moved. Cases of severe mustard-gas intoxication were also sent to building B inasmuch as this was the only building equipped with bathing facilities. Each of the four large buildings had in one end, on the lower floor, what was called the "bathroom," but these rooms were only equipped with small faucets, and there were no facilities for bathing. In the building B, however, a French portable bath had been installed in the bathroom, and this shower would bathe six persons standing, but only one lying. It was evident that no large number of cases could be handled, and another portable shower that would bathe eight persons standing was installed before the first patient was admitted.

Building A was set aside for officers and for the less severe cases of mustard-gas intoxication. Building B was set aside for walking cases in order to facilitate evacuations, and building C was the overflow ward.

EQUIPMENT

The equipment was supposed to be complete and was fairly complete according to the original French inventory, but some of the other hospitals on duty in the group had taken many of the supplies to make up for their own deficiencies before these buildings had been specified for hospital purposes.

There were about 700 beds that had been left by the French. These were iron beds with boards in place of springs and mattresses made of straw. These mattresses were clean and had been recently sterilized. There were sheets and blankets for making up the beds, but not enough sheets for changes. There were very few towels and pajamas. There were sufficient cooking utensils and dishes to meet the emergency, but they were not adapted to our needs. There were enough bedpans, urinals, etc., to meet the requirements.

The pharmacy was stocked with a large variety of excellent drugs and dressings and later, when medical cases were admitted, as well as gas cases, this proved to be a most fortunate acquisition. In these early days many difficulties presented themselves, and some of them were never entirely overcome.

ADMINISTRATION

There was a lack of clerks and stenographers. It was attempted to make up for this lack by appealing to the other units on duty in the group, but the men that were sent were inexperienced, and at no time did the hospital have a man that could do any of this work satisfactorily. It was necessary for the officers to do much of the typewriting, and the record work had to be constantly supervised.

There was no office equipment. Everything had to be purchased in the open market. There were no typewriters available with the exceptions of two small machines that officers attached to the hospital had brought with them. It was not until the middle of September that a standard machine was obtained, and that was borrowed from an individual.

Blank forms were difficult to obtain, and inasmuch as it was late in the month before they were obtainable, this added much to the necessary typewriting.

ENLISTED PERSONNEL

The enlisted men from the special training battalion were all classified as class B men, and none of them was strong and vigorous. Ten of the number were not physically equal to the demands that were made on the others. None of them had ever been attached to the Medical Department, and none of them had any special qualification that made him useful to the hospital. It was evident from the start that each man would have to be taught the particular work he had to perform. The majority of the men did not enter into the work with enthusiasm, and their discipline was very poor. They were very much disgruntled, and the idea of working with the Medical Department was not pleasing to them.

For the first 10 days it required constant watching in order to get the work performed; it meant constant disciplinary action to make them realize the task that was before them. After this time, however, the majority of them worked faithfully and cheerfully, and it is in a large measure due to the strained efforts of these men that the hospital was a success.

Nine enlisted men were assigned to the hospital from another unit in the group to act as noncommissioned officers, but these men, for the most part excellent, had not been trained, and it was hardly to be expected that under the circumstances another organization would voluntarily give up its best men.

It was hoped that these deficiencies would be overcome in a large measure by the employment of civilian help, and especially in the kitchen, but it was soon found that the French cooks were not accustomed to our methods of cooking, and they were far from being in sympathy with our ideas of sanitation. It was necessary to let them go and begin training our own men to cook.

Difficulty was experienced with all of the civilian help with the exceptions of the woman in the pharmacy, the woman in charge of the linen room, and the seamstresses. All these women proved to be very valuable.

SUPPLIES

In the early days of the group the problem of supplies was a serious one. There was not enough to go around, and division on a basis of equality, according to needs, was attempted, but did not work out very satisfactorily. Our supply officer had various duties and could give only a portion of his time to this duty. The other hospitals had their supply officers, who were constantly on the alert. This was compensated in a large measure by the fact that Lieutenant Wilder had seen long service in France and knew better what was wanted and where to get it than most of the other supply officers. The spirit of the moment is well illustrated by the notation that there was a tendency on the part of some officers to help themselves to whatever they wanted, regardless of where they saw it. On one occasion a noncommissioned officer was found removing a valve from our shower bath, and it was necessary for the man in charge of the bath to call an officer before he could be induced to stop. He was found to be acting under orders from a superior officer.

KITCHENS

The kitchens were inadequate, even with the repair of the second French range. Fortunately gas cases are given nothing but liquid foods in the early days of their treatment, so that the only ones suffering from the deficiency were the personnel of the hospital.

With the installation of the Army range much better service was rendered, although another range should have been set up in order to render the service that should have been rendered. Effort was made to prepare food, especially hot, liquid food, in the various buildings, but it was late in September before small stoves were obtainable and some time later before oil could be procured.

WATER SUPPLY

The water supply was very limited and so much so that in running the bath it was necessary to see that the bath was used at its full capacity at the hours during which bathing was permitted. It was planned to be able to give baths to the cases of mustard-gas intoxication whenever they came in, and we were able to do this throughout the life of the hospital. This would not have been so had all the cases required bathing. This was obviated by the preliminary treatment given at the field hospitals.

Several times the water supply was entirely cut off on account of shortage of water, but by keeping a reserve in the bathroom it was possible to see that all necessary treatment was given.

Again, the spirit of the moment was seen when an officer from another unit cut the tank of the gas hospital area out of the circuit during pumping hours, hoping to get the extra amount in his own tank. Fortunately, the water system was so arranged that any interference with the supply system made itself evident throughout the group and the trick was discovered.

None of the water was safe for drinking purposes, and it was all boiled or chlorinated before it was used. This matter was under the constant supervision of one of the officers, and no case of illness due to the water occurred at the hospital.

WASTE MATTER

A good deal of trouble was experienced in getting the latrines emptied and the garbage carried away. At one time the situation was so bad that trenches for disposing waste matter were dug, but it was never necessary to use them. Before the rush of work came the contractors were more regular in their work, but at no time was it entirely satisfactory.

LIGHTING

The hospital was lighted with electricity and for the most part the service was good. It was, of course, necessary to camouflage the entire plant; and although a good deal of difficulty was experienced in getting the necessary materials to do this work, it was completed before the activities began. Here again it was necessary for the officers to personally put up the first covers and teach the men in order that the work could be completed.

By September 7, the hospitals were fairly well equipped and supplied; the men had been assigned to their various duties and had been started in their training. The entire plant has been camouflaged and everything was ready for action.

About 7 p. m. on this date brilliant flashes of light and sounds of heavy firing was seen and heard in the north. The firing continued at intervals all the next day and at 4 p. m. on September 8, the first patient, Second Lieut. Paul Odom, Company D, 341st Machine Gun Battalion, arrived and was diagnosed as phosgene-gas intoxication, slight.

On September 8, 15 nurses were assigned to the hospital for temporary duty per S. O. 40, Headquarters, J. H. G. These nurses were attached to Base Hospital No. 45, and while they were quartered at the gas hospital they were messed and carried on all reports and returns of their own organization.

* * * * *

On September 11, Capt. Paul Dejains, Evacuation Hospital No. 2, reported at headquarters, Justice hospital group, in compliance with telegraphic orders of the commanding general of the First Army. He was assigned to duty with the gas hospital.

At 7. p. m. on the evening of September 11, commanding officers of the various hospitals were called to group headquarters and informed that activities were to begin in the St. Mihiel sector within 24 hours, and we were given our final instructions as to preparations for the drive. About 12 hours later the activities in the north, which could be distinctly seen, heard, and felt, indicated that the drive had begun. The next morning cases began to come to the group over the road, but only one case was admitted to the gas hospital on September 12 and only 38 cases on September 13. All these cases had been sent back from field hospitals. The early rumors were to the effect that little or no gas was being used. By this time it was evident that the gas hospital was destined to act as an evacuation hospital and there would be comparatively little initial treatment here. For this reason Captain Dejains returned to his hospital, Evacuation No. 2, the night of September 12.

First Lieut. William J. Kane, M. C., Evacuation Hospital No. 14, reported for duty on September 12, 1918, as per S. O. 45, Hdqrs., Justice hospital group, but was relieved by S. O. 63, Hdqrs., J. H. G., September 19, 1918.

On September 14 General Gorgas made an official inspection of the hospital. On the afternoon of September 18, cases began to arrive at the hospital in large numbers; and from 12 o'clock noon on the 17th until 12 o'clock noon on the 18th, 416 cases were admitted and 466 cases were evacuated. Fortunately, the few cases that had been coming into the hospital in the five previous days had given the personnel some experience in the duties that they had to perform, otherwise the mechanism of the hospital would have broken down with this large number of cases that had to be handled by this small number of men. During the evening and also during a very active period, General Gorgas made an unofficial visit and watched the operation in the triage with much interest, after which he made a rather complete visit of the wards. His interest seemed to be entirely in the soldier, as he was critical of the attention given to the men in the triage, making special note as to the methods of keeping them warm, feeding them, and of the initial medical treatment that they were receiving. On the morning of the 18th, it was evident that this small force could not keep on with the work, and in consequence 40 additional enlisted men from the same special training battalion reported for duty on the evening of September 18, 1918.

* * * * *

On the afternoon of September 18, 1918 * * *. These officers were ordered to report for duty to this group from the schools at Langres. It was not possible to have the advantage of their undivided service as each had to spend a part of the time at this headquarters in service at the front. The uncertainty of their service made it undesirable to assign administrative work to them, but they rendered most excellent medical service, and arrived just in time to prevent disaster owing to lack of officers.

It was on this same day that the hospital was instructed to admit medical as well as gas cases. At this time a severe epidemic of influenza had made its appearance, and owing to the crowded condition in the other hospitals it was necessary to admit some of the cases to the gas hospital. This presented a rather serious problem owing to the danger to gas cases of secondary infection. All of the respiratory gas cases were immediately segregated, and in so far as possible the cases of influenza were isolated.

The installation of cubicles was immediately begun and, while materials were lacking, the work was pushed as rapidly as possible, cubicled observation wards being established in each building within 24 hours.

After September 20, the number of gas cases admitted began to diminish and the number of medical cases to increase. Medical cases were almost entirely respiratory and enteric. On September 25, Maj. Albert Francine, M. C., reported for duty as per S. O. No. 81, Hdqrs. J. H. G., and was assigned as assistant chief of the medical service. On the same date First Lieut. Walter F. Bleifus, M. C., Base Hospital No. 78, was assigned to duty in compliance with S. O. No. 88, Hdqrs. J. H. G. On September 30, 1918, First Lieut. John W. Blake, M. C., Base Hospital No. 55, was assigned to duty as per S. O. No. 106, Hdqrs. J. H. G. Both of the last-named officers became ill shortly after they reported for duty and were not available again for service.

About this time a rather severe epidemic of pneumonia, due to the streptococcus hemolyticus, made its appearance and assumed severe proportions. The severity of the epidemic added very much to the work of the very limited personnel, both officers and men, and repeated attempts to have more officers, nurses, and men assigned to the hospital were made but the demand was so great in other units of the group that none could be spared, and on October 8, 1918, the patients and property of the hospital were turned over to Base Hospital No. 87, which had just arrived in the group.

Inasmuch as the hospital was originally intended for the treatment of gas cases, the summary will only touch on that subject. The work done by the hospital is shown by the following table:

	Cases admitted	Gas cases	Cases evacuated		Cases admitted	Gas cases	Cases evacuated
Sept. 10.....	1	1	0	Sept. 26.....	70	70	0
11.....	1	1	0	27.....	70	46	109
12.....	1	1	0	28.....	0	0	0
13.....	38	38	0	29.....	53	30	0
14.....	19	19	56	30.....	196	80	0
15.....	11	11	0	Oct. 1.....	254	86	0
16.....	21	21	0	2.....	215	15	145
17.....	85	85	0	3.....	0	0	9
18.....	416	320	466	4.....	1	1	1
19.....	462	101	66	5.....	20	19	5
20.....	105	69	0	6.....	26	11	9
21.....	97	28	45	7.....	20	10	95
22.....	0	0	644		167	139	5
23.....	0	0	62				
24.....	37	37	77		2,587	1,351	1,829
25.....	211	112	35				

The gas cases were classified as follows:

Mustard.....	828	Chloropicrin.....	26
Phosgene.....	191	Gasoline fumes.....	8
Undetermined.....	105	Mustard and phosgene.....	8
Shell fumes.....	70	Chlorine.....	7
Arsene.....	38		
			1,281

Of this total number of cases, only 169 came directly from the front, and these found their way by accident and were not sent back by medical direction. There were but 5 deaths, all following intoxication with mustard gas. Post-mortem examinations were made and showed the following condition:

Pvt. Hels Malgren, 2855737, Company D, 360th Infantry, died September 24, 1918. The autopsy showed marked burns about the eyes and mouth, burns on the forearms, scrotum, and buttocks. Beginning at the larynx and extending down the entire trachea was a thick, frothy, greenish-gray membrane covering the entire mucous membrane. This was easily removed. There was marked hyperemia and edema of the pulmonary tissues. Scattered throughout both lobes were many dark red, almost black, areas of consolidation. The bronchi were filled with a greenish, purulent material extending down to the smallest bronchioles. Anatomical diagnosis: Gas intoxication, severe, mustard; bronchopneumonia.

Marius Albade (French), private 151st Regiment 6A, October 2, 1918: Conjunctivæ hyperemic. Around the eyes, over the lips, and around the nose the skin is ulcerated and covered with a thick red scab. Similar excoriation on the scab over scrotum. Areas of broncho-pneumonia in both lungs. The bronchi contained pus and the mucous membrane from the primary bronchi to the smallest bronchioles were covered with a thick green membrane. Anatomical diagnosis: Gas intoxication, severe, mustard; bronchopneumonia.

Charles Beneck (French), private, 151st Infantry, F. A., October 2, 1918: Thick brownish red scabs around the eyes, lips, and nose. External genitals hyperemic. Areas of

bronchopneumonia in both lungs. The bronchi contained pus and the mucous membrane from the primary bronchi to the smallest bronchioles were covered with a thick greenish membrane. Anatomical diagnosis: Gas intoxication, severe, mustard; bronchopneumonia.

Private Fred Hoffman, 93596, Company D, 166th Infantry, October 3, 1918: Conjunctivæ congested. Some excoriated areas around the eyes, nostrils, and mouth. The larynx and trachea were covered with a thick yellowish membrane. Areas of broncho pneumonia in both lungs. Anatomical diagnosis: Gas intoxication, severe, mustard; bronchopneumonia.

Private Robert Grundon, 93377, Company D, 166th Infantry, October 8, 1918: Conjunctivæ red. The skin around the eyes, nose, and mouth covered with a thick adherent reddish scab. Similar scabs around the genitals. Pharynx and soft palate covered with a thick greenish membrane. A similar membrane extended from the epiglottis to the finer bronchi. There was a large amount of bloody froth in the trachea. Lungs hyperemic. Anatomical diagnosis: Gas intoxication, severe, mustard.

Some very interesting facts developed in this very short experience. Unfortunately there was not time to take careful notes and collect statistics, but many of the patients were closely questioned, and the general impression is probably not very far from correct.

First of all, one is impressed by the fact that the large majority of the cases, fully 75 per cent, were not severely gassed. Of this number 20 per cent were probably not gassed at all. They were rather victims of exhaustion, shell fume, etc. Fully 25 per cent of the cases could have been returned to duty within 24 hours, and fully 50 per cent could have been returned to duty within from four to six days. Of the 828 mustard-gas cases the 5 that died were the only cases that were considered seriously ill. In only about 20 per cent of the mustard cases was the condition severe enough to confine the patient to bed for more than 48 hours.

The division between respiratory cases and contact mustard-gas cases was about equal. While some of the skin burns were severe and extensive, in none did it appear that the healing would be prolonged to any degree. The eyes were affected in about 40 per cent of the cases to a degree to require treatment, but the rapidity with which they improved was surprising, and in no case was there real danger to the sight.

In about 20 per cent of all the cases the diagnoses were by no means certain. They had been sent back with a diagnosis of mustard-gas intoxication. On the field card the history was mustard-gas intoxication, but the signs at the time of admission were the ones that one might expect of man's being exhausted. They had been without sleep and their eyes had been irritated by dust.

Of the phosgene cases, less than 12 were sick enough to be confined to bed for more than two days, and in only one case was it necessary to do a phlebotomy. Of the other cases of the gas intoxication, none was sick enough to require any treatment. The cause of the casualty was always determined in the general way, and it is the opinion of the officers of the hospital that the great majority of the casualties was the lack of discipline in the use of the gas mask and the lack of precaution against gas bombardment. Many of the men said that they took their masks off, as they would rather take a chance without it than fight with it on. A good number had their masks knocked off in one way or other. Some admitted that their masks were defective and that they knew it before going into action. One convoy that was brought in was shelled in the night and caught in the dugout. No alarm was sounded until it was too late to protect themselves.

Several of the more severe contact cases were seen in men who were burned in helping their comrades out of danger, or who had taken cover in a shell hole that was contaminated.

The work done at this hospital was in reality work that could have been handled in any of the units of the group. Had the cases that were admitted to the hospital been cases requiring initial treatment, the personnel and the equipment would not have been sufficient to have rendered proper service. It is believed, however, that this particular hospital served a very useful purpose, possibly a service that none of the others could have rendered, and that is the isolation and protection of respiratory gas cases from accidental secondary respiratory infections.

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